Special Edition

Gastrointestinal Anatomy and Motility

Selections from the
Netter Collection of Medical
Illustrations

F. Netter M.D.

Netter's Gastrointestinal Anatomy and Motility

Frank H. Netter, MD

Selections from the Netter Collection of Medical Illustrations

Text by
William [illegible], MD, PhD

Netter's Gastrointestinal Anatomy and Motility

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Selections from the Netter Collection *of* Medical Illustrations

Text by
William H. Bachrach, MD, PhD

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FOREWORD
Frank Netter: The Physician, The Artist, The Art

This selection of the art of Dr. Frank H. Netter on gastrointestinal anatomy and motility is drawn from *The Atlas of Human Anatomy* and *The Netter Collection of Medical Illustrations*. The choice of subject matter is particularly appropriate given Dr. Netter's training as a surgeon and his continuing interest in the subject. Viewing these pictures again four decades after their original publication prompts reflection on Dr. Netter's work and his roles as physician and artist.

Frank H. Netter was born in 1906 in Brooklyn, New York. He pursued his artistic muse at the Sorbonne, the Art Student's League, and the National Academy of Design before entering medical school at New York University, where he received his M.D. degree in 1931. During his student years, Dr. Netter's notebook sketches attracted the attention of the medical faculty and other physicians, allowing him to augment his income by illustrating articles and textbooks. He continued illustrating as a sideline after establishing a surgical practice in 1933, but ultimately opted to give up his practice in favor of a full-time commitment to art. After service in the United States Army during the Second World War, Dr. Netter began his long collaboration with the CIBA Pharmaceutical Company (now Novartis Pharmaceuticals). This 45-year partnership resulted in the production of the extraordinary collection of medical art so familiar to physicians and other medical professionals worldwide.

When Dr. Netter's work is discussed, attention is focused primarily on Netter the artist and only secondarily on Netter the physician. As a student of Dr. Netter's work for more than forty years, I can say that the true strength of a Netter illustration was always established well before brush was laid to paper. In that respect each plate is more of an intellectual than an artistic or aesthetic exercise. It is easy to appreciate the aesthetic qualities of Dr. Netter's work, but to overlook its intellectual qualities is to miss the real strength and intent of the art. This intellectual process requires thorough understanding of the topic, as Dr. Netter wrote: "Strange as it may seem, the hardest part of making a medical picture is not the drawing at all. It is the planning, the conception, the determination of point of view and the approach which will best clarify the subject which takes the most effort."

Years before the inception of "the integrated curriculum," Netter the physician realized that a good medical illustration can include clinical information and physiologic functions as well as anatomy. In pursuit of this principle Dr. Netter often integrates pertinent basic and clinical science elements in his anatomic interpretations. Although he was chided for this heresy by a prominent European anatomy professor, many generations of students training to be physicians rather than anatomists have appreciated Dr. Netter's concept.

The integration of physiology and clinical medicine with anatomy has led Dr. Netter to another, more subtle, choice in his art. Many texts and atlases published during the period of Dr. Netter's career depict anatomy clearly based on cadaver specimens with renderings of shrunken and shriveled tissues and organs. Netter the physician chose to render "live" versions of these structures—not shriveled, colorless, formaldehyde-soaked tissues, but plump, robust organs, glowing with color!

The value of Dr. Netter's approach is clearly demonstrated by the plates in this selection, which maintain a level of accuracy and clarity that belies their years. The original text has been edited only slightly. Although much has been learned on the subject of gastrointestinal motility since it was written, most of the fundamental principles it describes are still sound.

John A. Craig, MD
Austin, Texas

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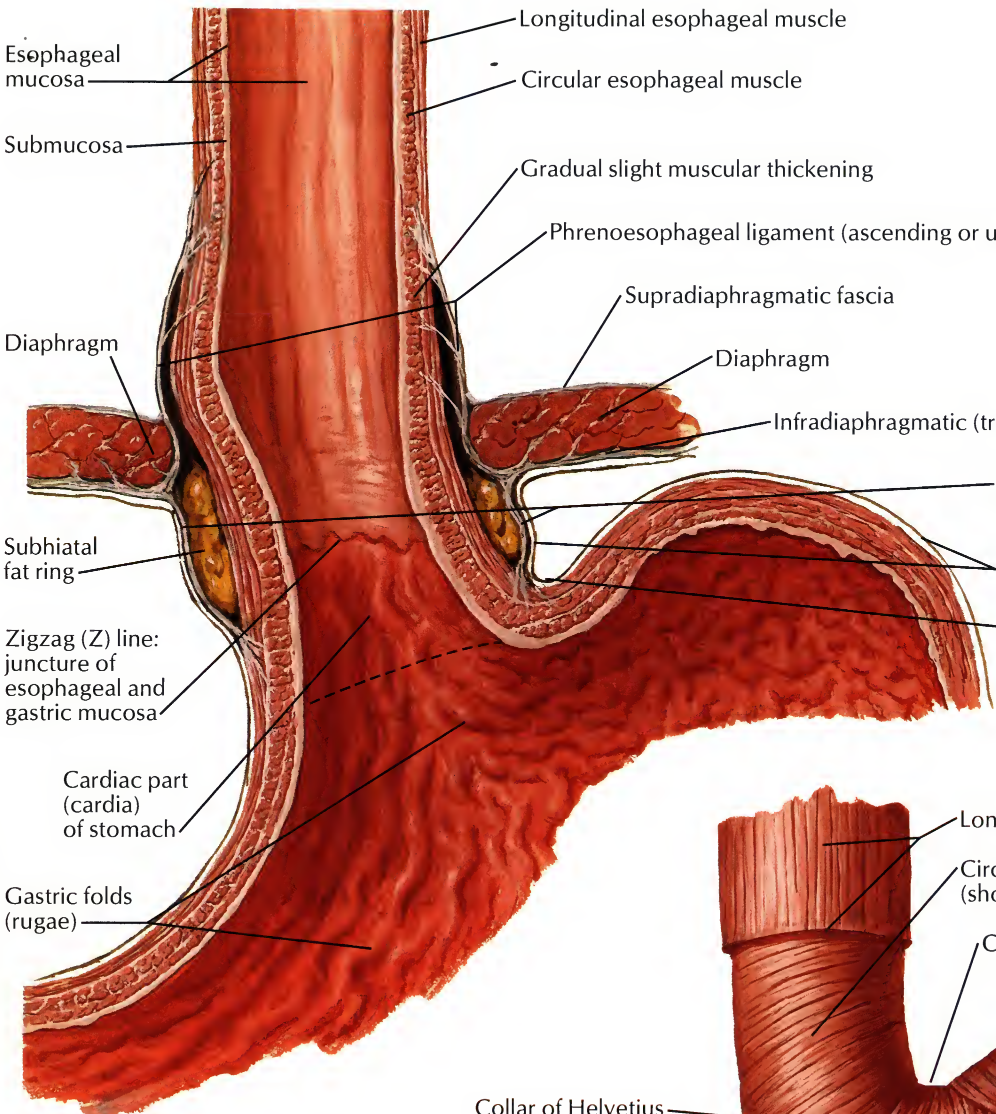
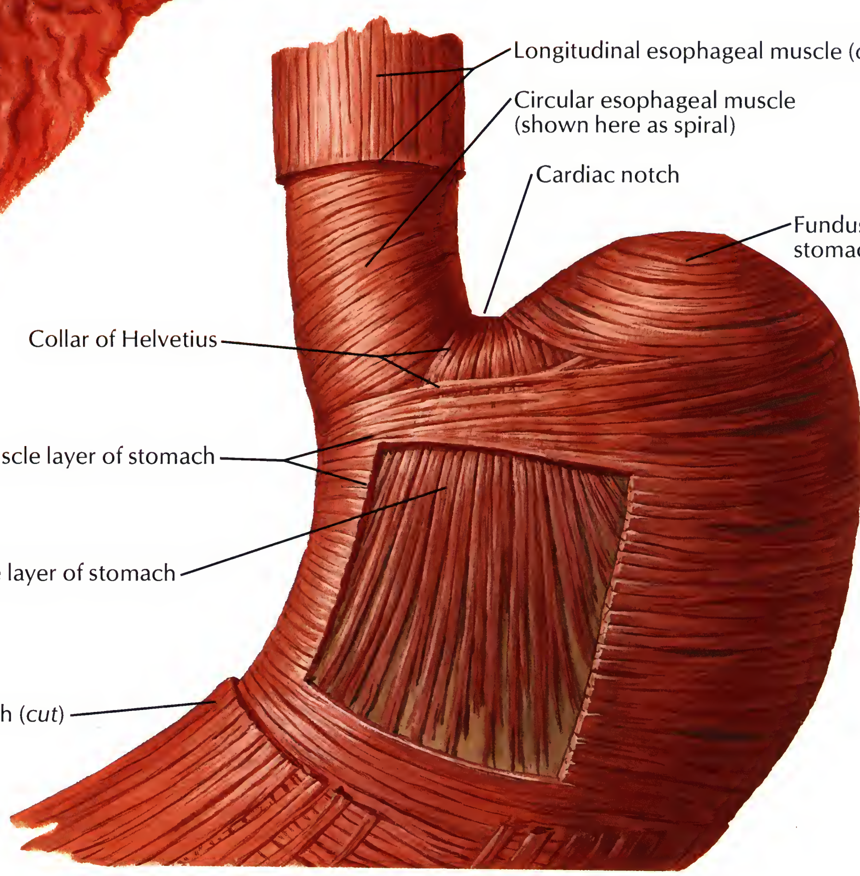
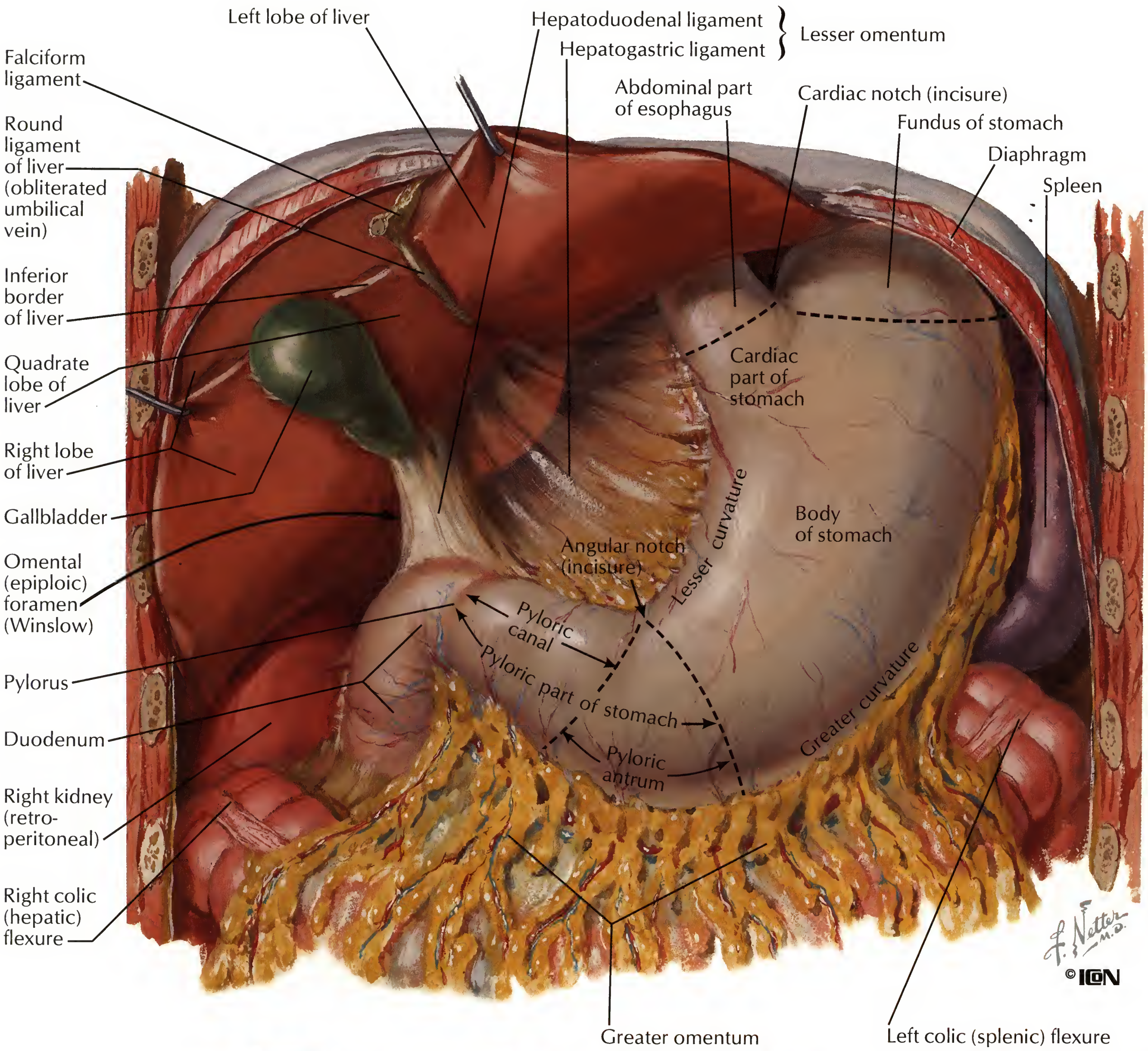
Anatomy of the Lower Gastrointestinal Tract

Functional Aspects of the Gastrointestinal Tract and Gastrointestinal Motility

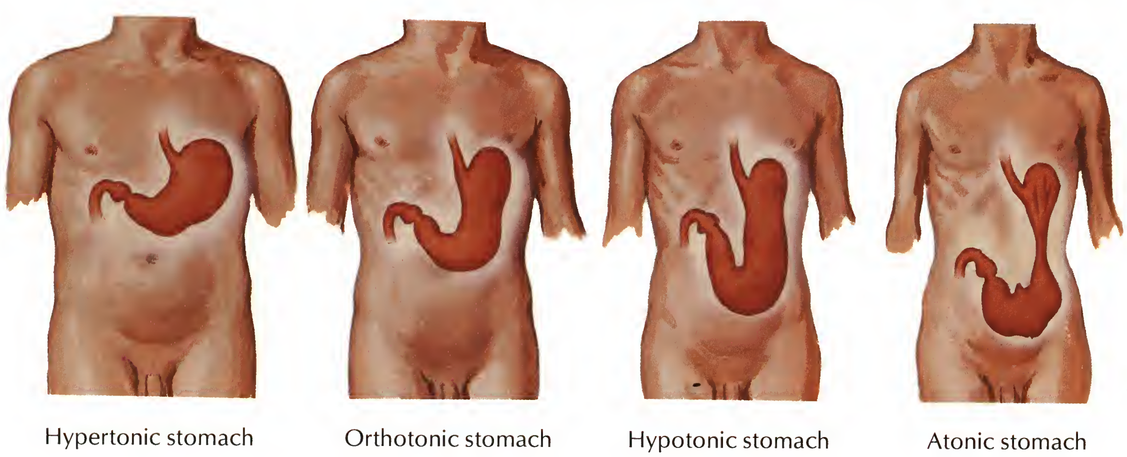
Esophagogastric Junction



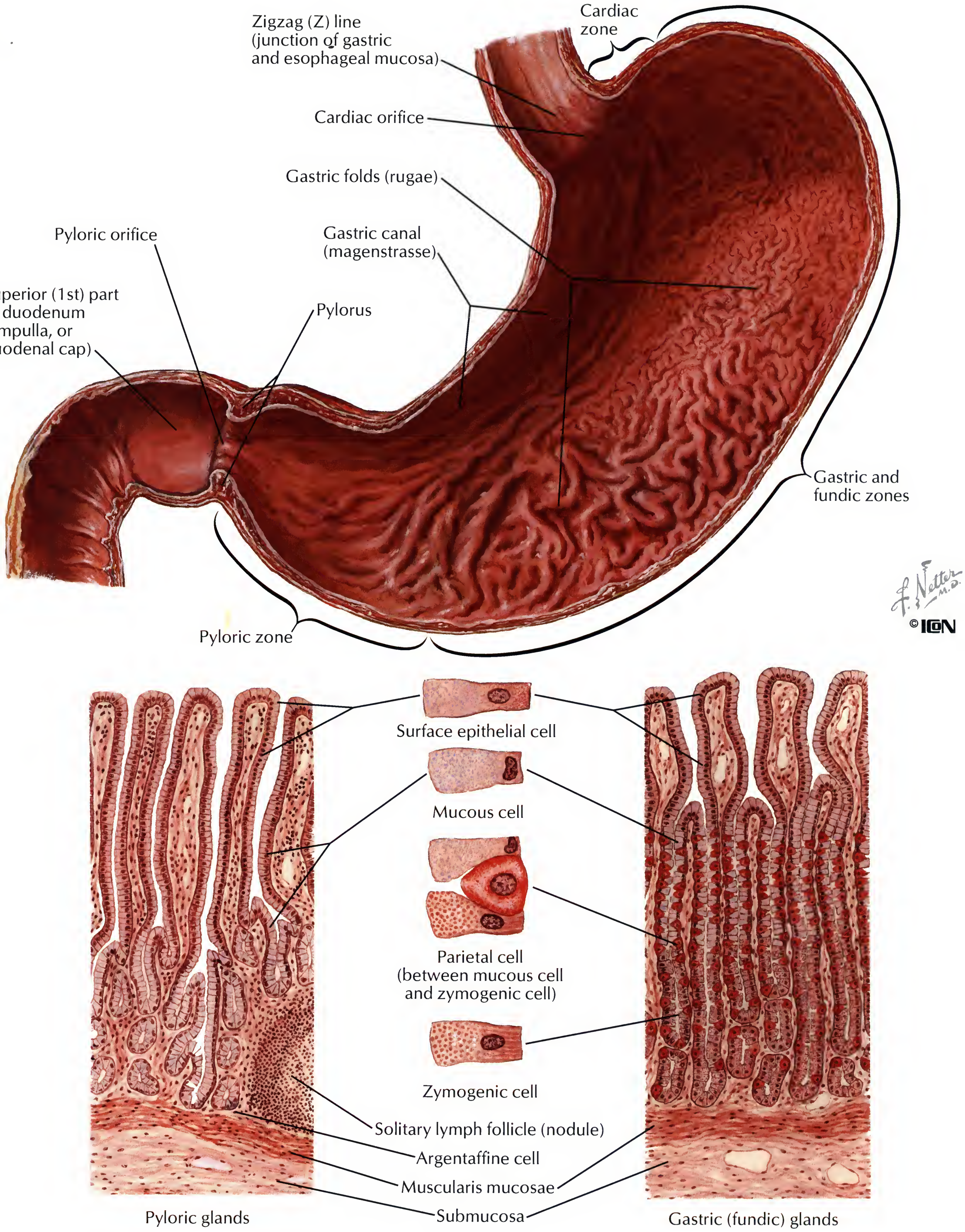


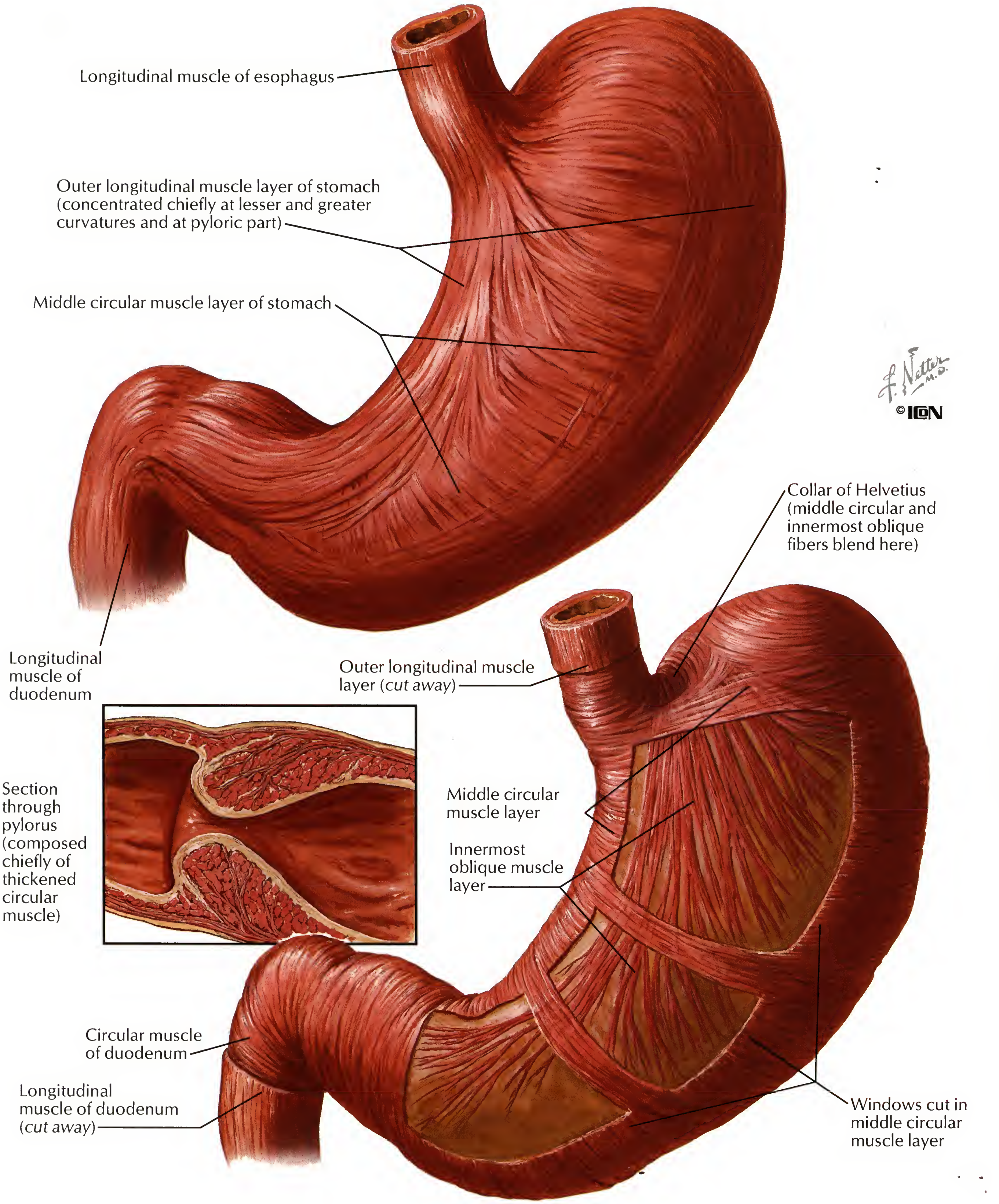


Variations in position and contour of stomach in relation to body habitus



Mucosa of Stomach




Longitudinal muscle of esophagus
Outer longitudinal muscle layer of stomach (concentrated chiefly at lesser and greater curvatures and at pyloric part)
Middle circular muscle layer of stomach
Longitudinal muscle of duodenum
Collar of Helvetius (middle circular and innermost oblique fibers blend here)
Outer longitudinal muscle layer (*cut away*)
Section through pylorus (composed chiefly of thickened circular muscle)
Middle circular muscle layer
Innermost oblique muscle layer
Circular muscle of duodenum
Longitudinal muscle of duodenum (*cut away*)
Windows cut in middle circular muscle layer
F. Netter M.D.
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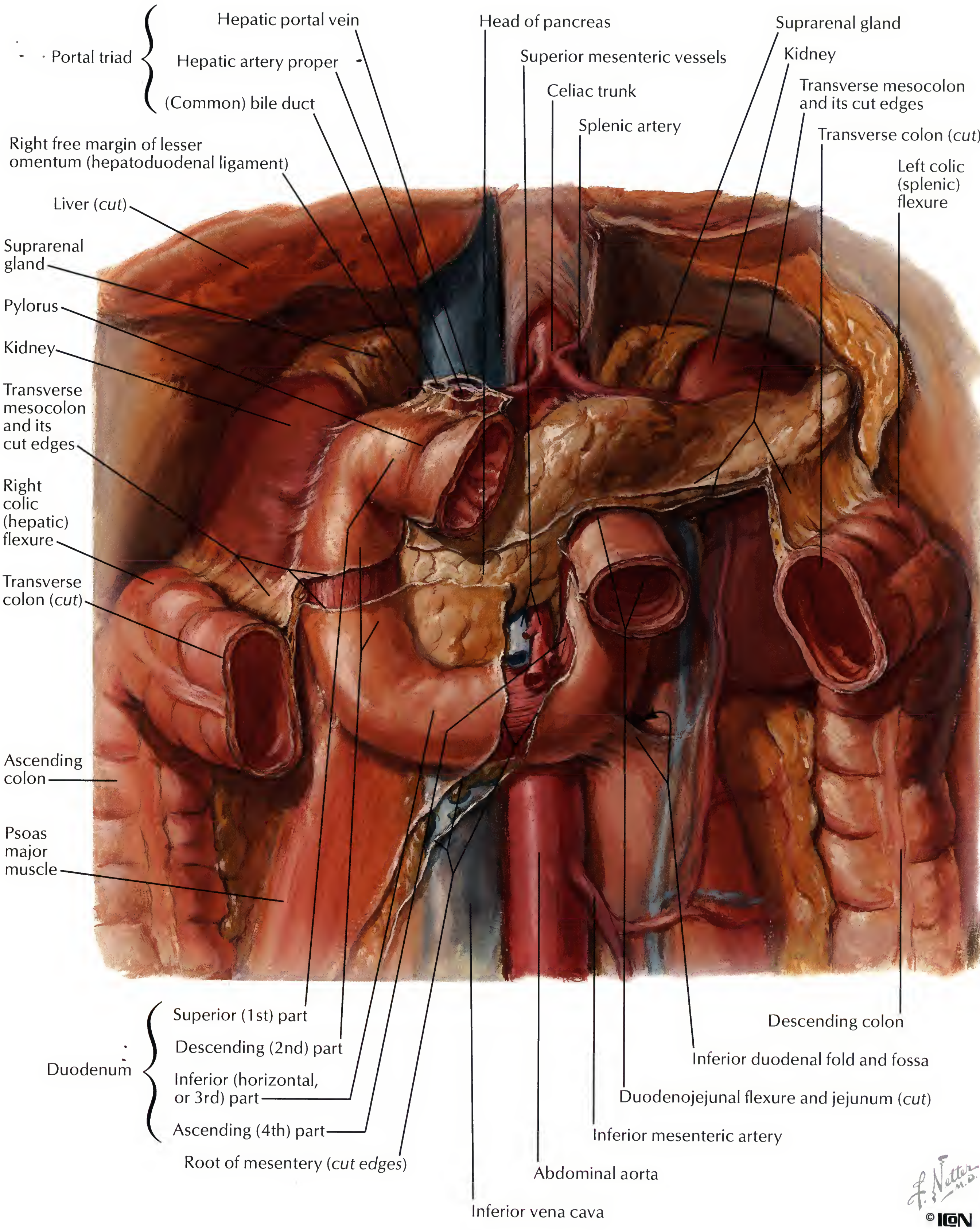
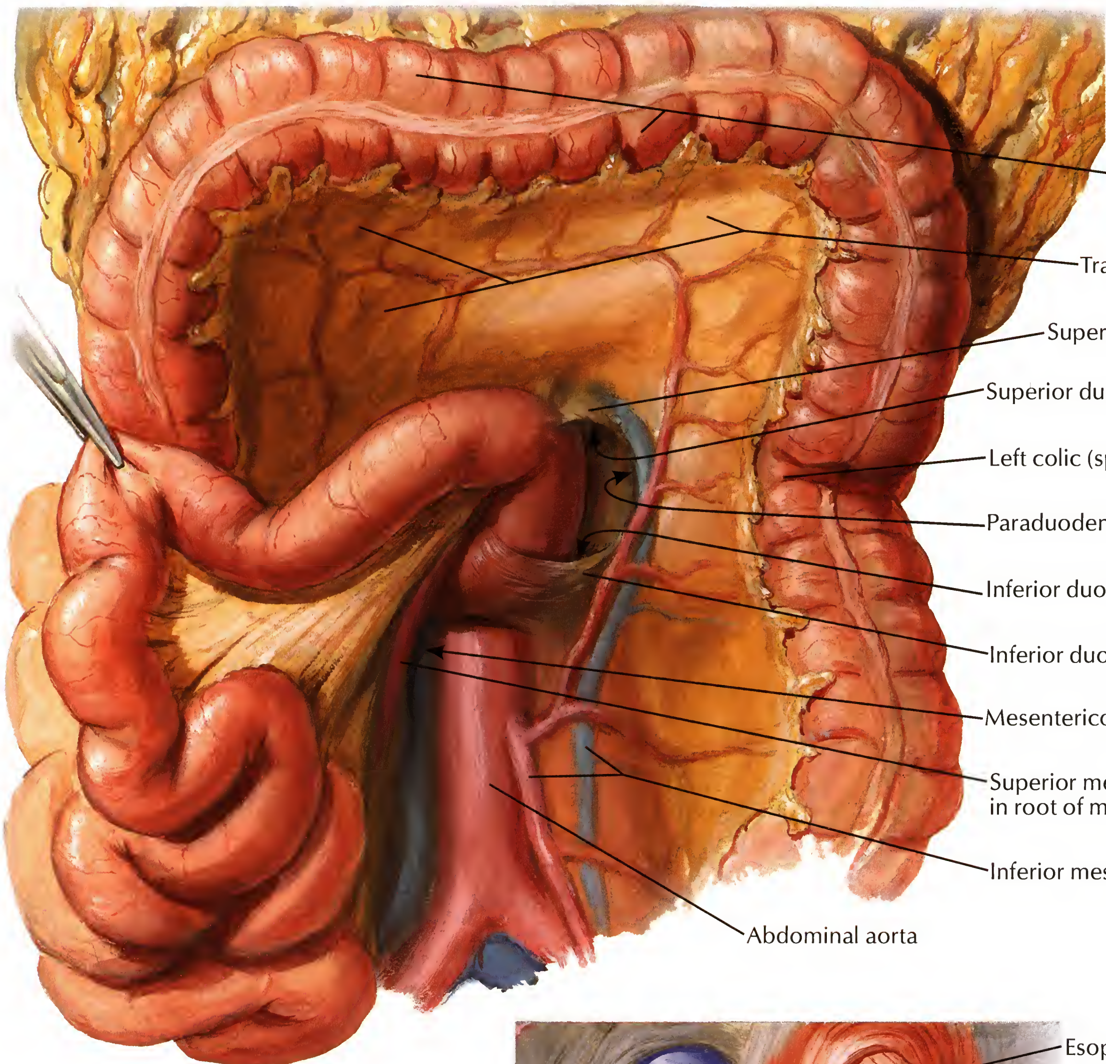
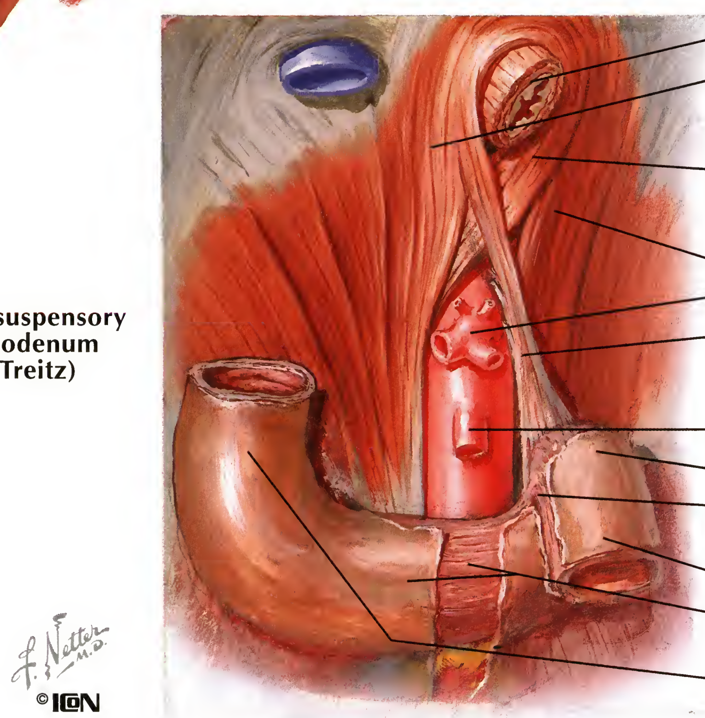
Duodenum in Situ

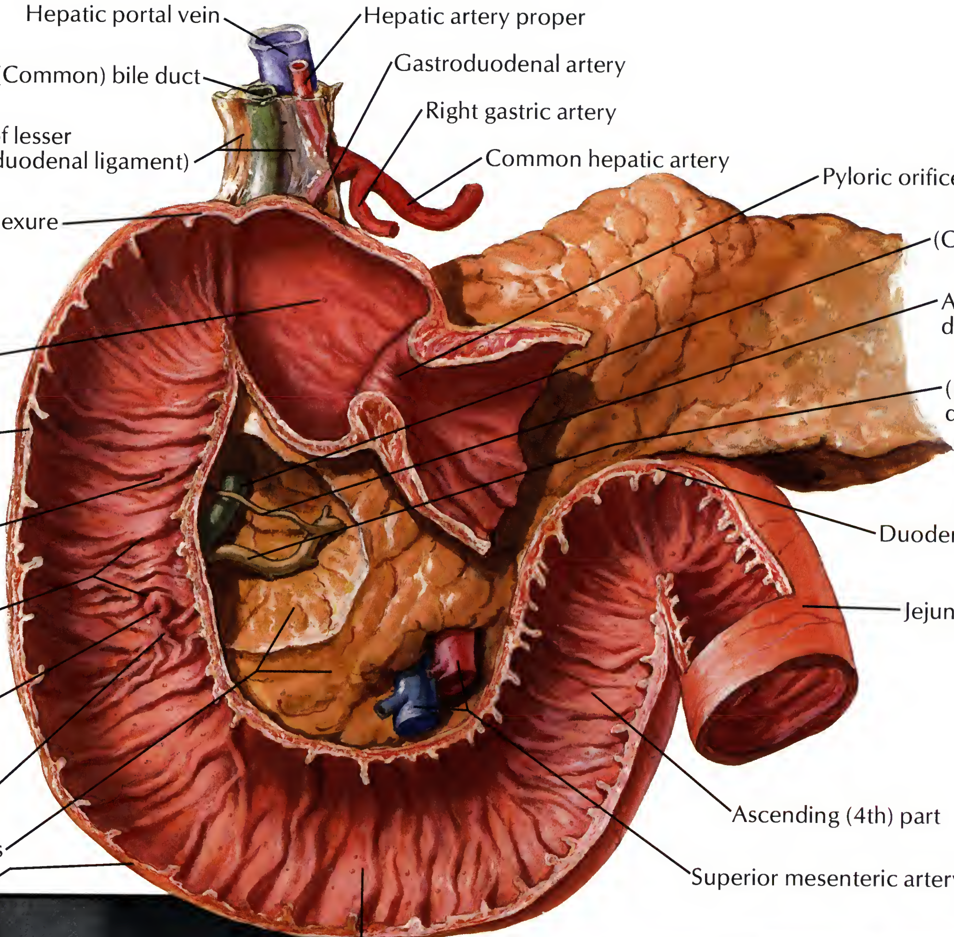




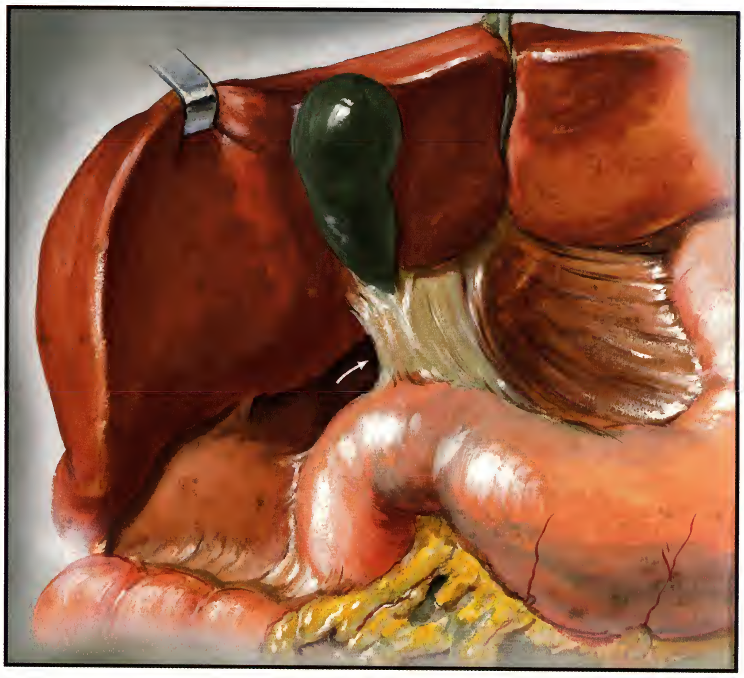
Exposure of suspensory muscle of duodenum (ligament of Treitz)



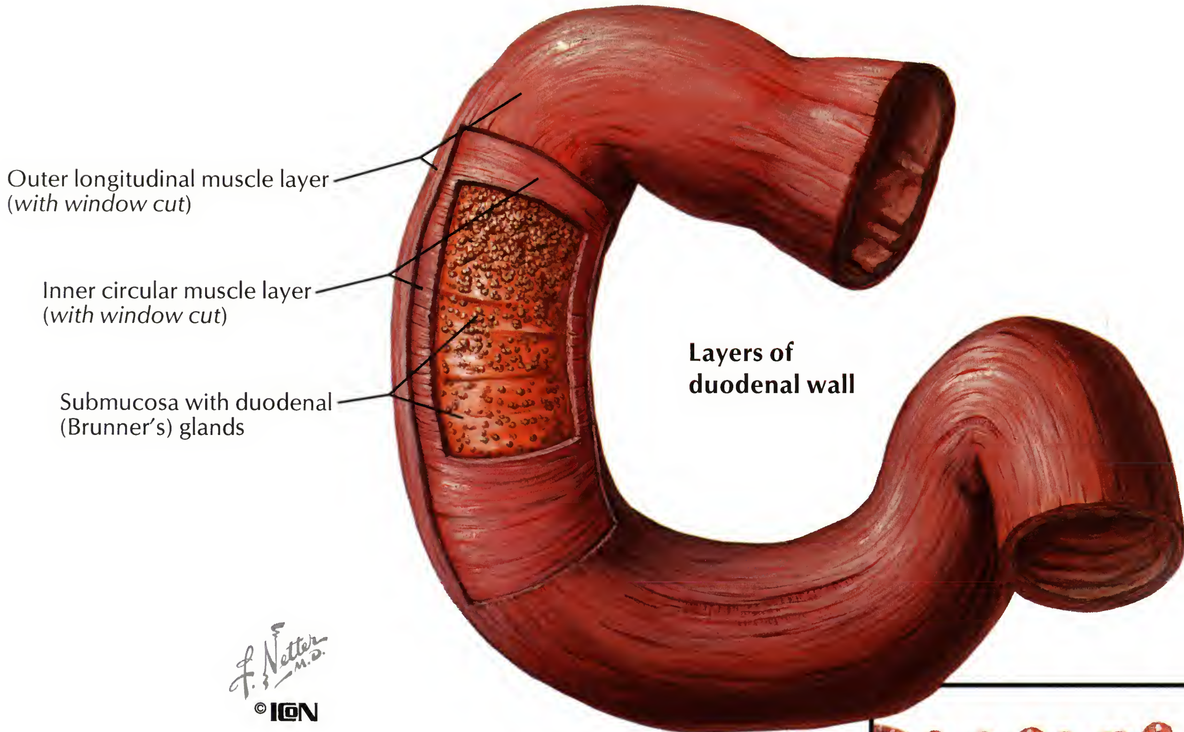
Duodenal Bulb and Mucosal Surface of Duodenum



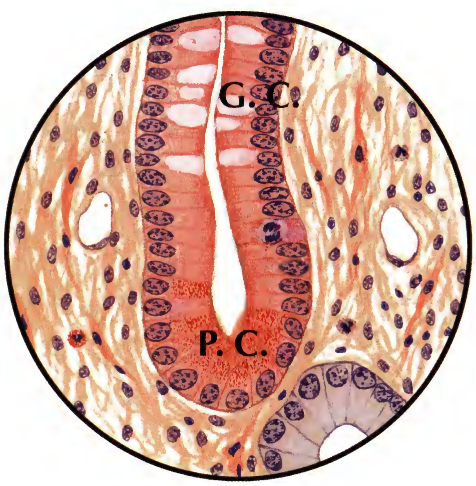
Normal Duodenal Bulb



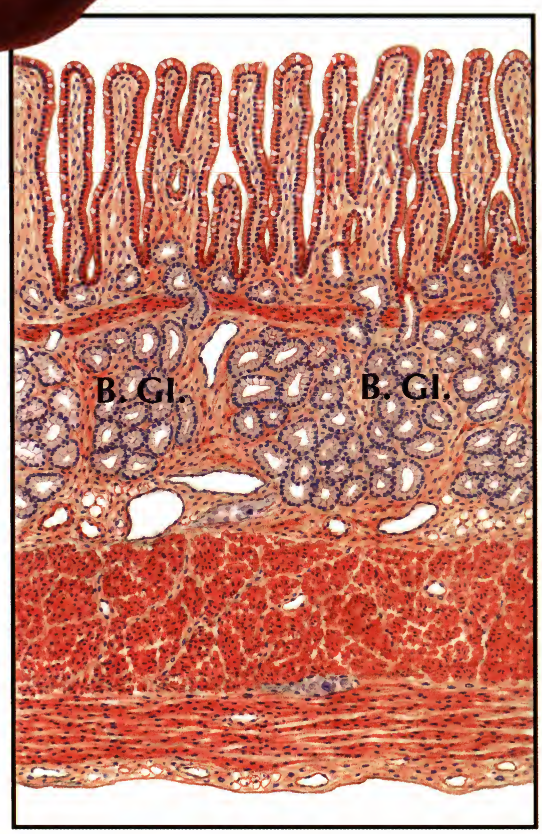
Foramen of Winslow



B. Gl. - Brunner's Glands
G. C. - Goblet Cell
P. C. - Paneth's Cell

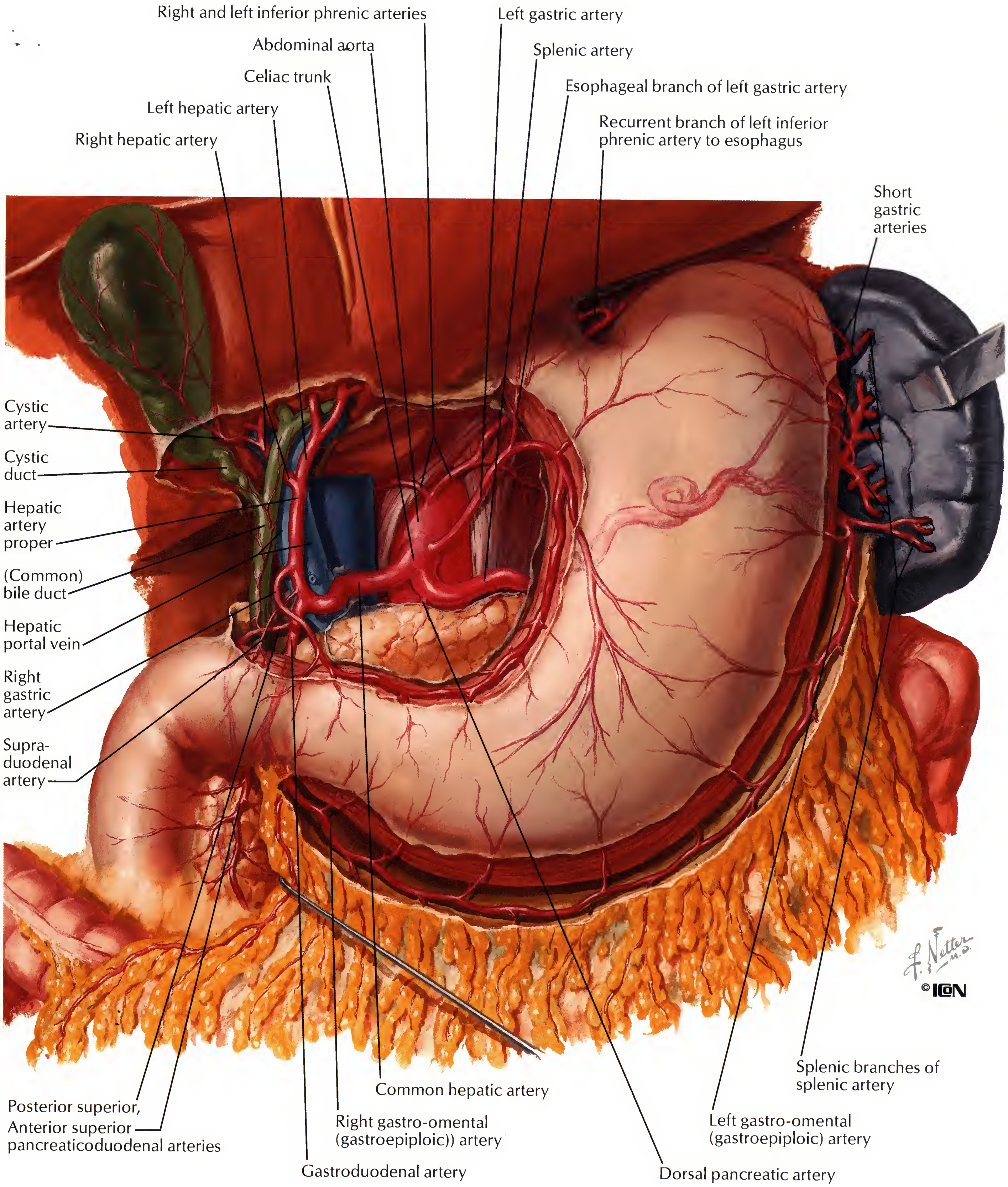


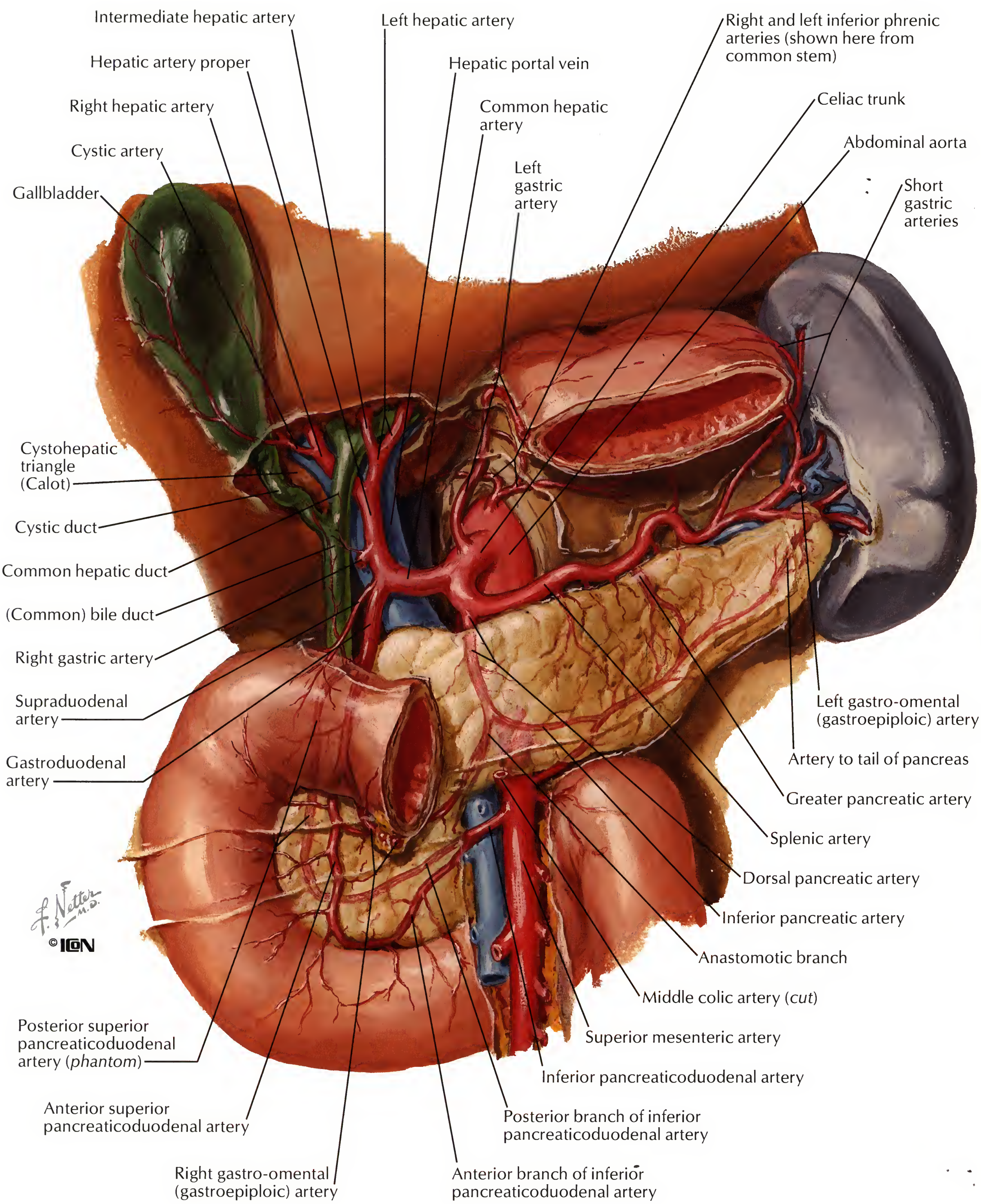
Crypt of Lieberkühn



Longitudinal Section Through Duodenal Wall

Arteries of Stomach, Liver, and Spleen




Intermediate hepatic artery
Hepatic artery proper
Right hepatic artery
Cystic artery
Gallbladder
Left hepatic artery
Hepatic portal vein
Common hepatic artery
Left gastric artery
Right and left inferior phrenic arteries (shown here from common stem)
Celiac trunk
Abdominal aorta
Short gastric arteries
Cystohepatic triangle (Calot)
Cystic duct
Common hepatic duct
(Common) bile duct
Right gastric artery
Supraduodenal artery
Gastroduodenal artery
Left gastro-omental (gastroepiploic) artery
Artery to tail of pancreas
Greater pancreatic artery
Splenic artery
Dorsal pancreatic artery
Inferior pancreatic artery
Anastomotic branch
Middle colic artery (*cut*)
Superior mesenteric artery
Inferior pancreaticoduodenal artery
Posterior branch of inferior pancreaticoduodenal artery
Anterior branch of inferior pancreaticoduodenal artery
Posterior superior pancreaticoduodenal artery (*phantom*)
Anterior superior pancreaticoduodenal artery
Right gastro-omental (gastroepiploic) artery
F. Netter M.D.
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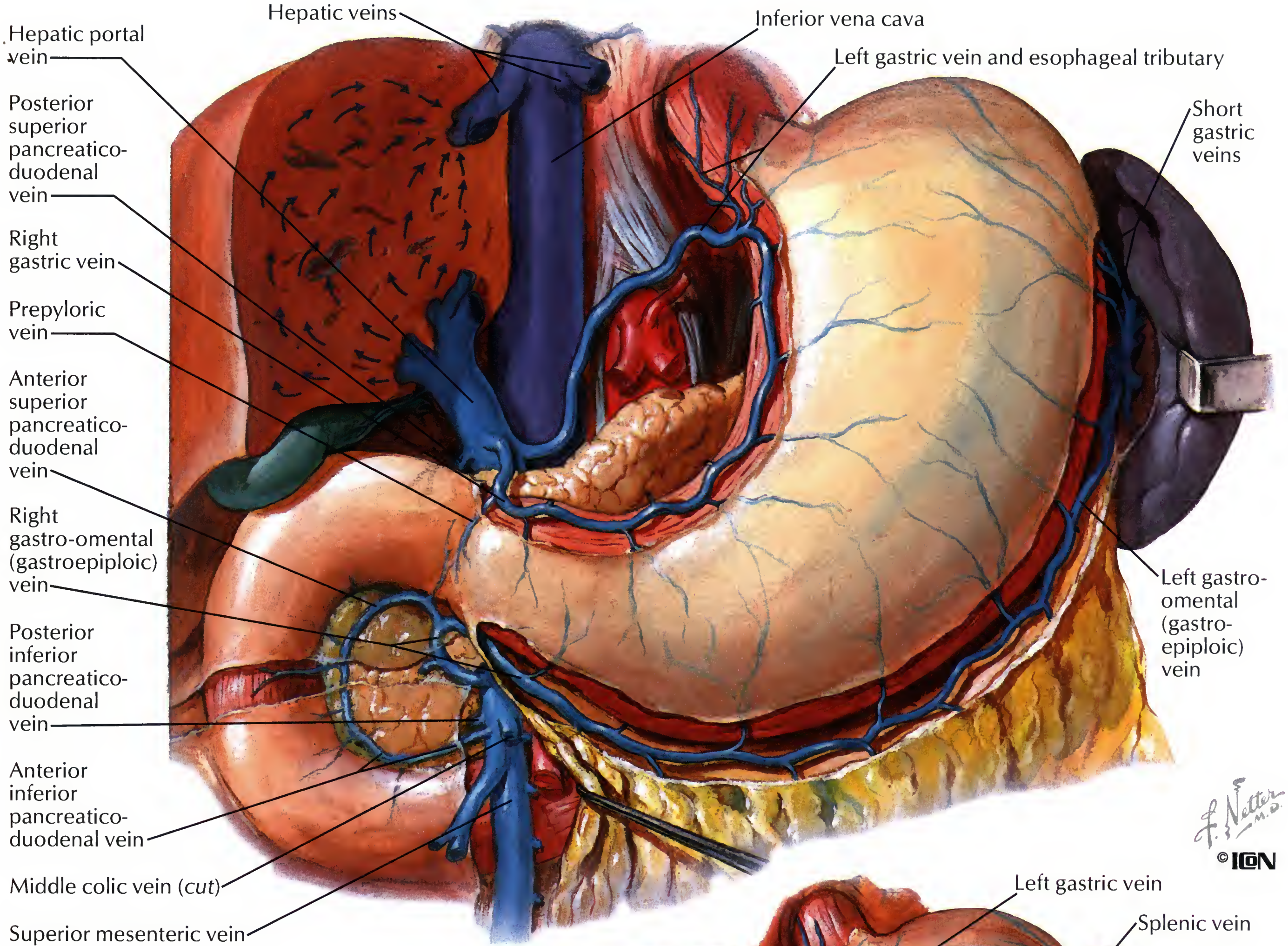
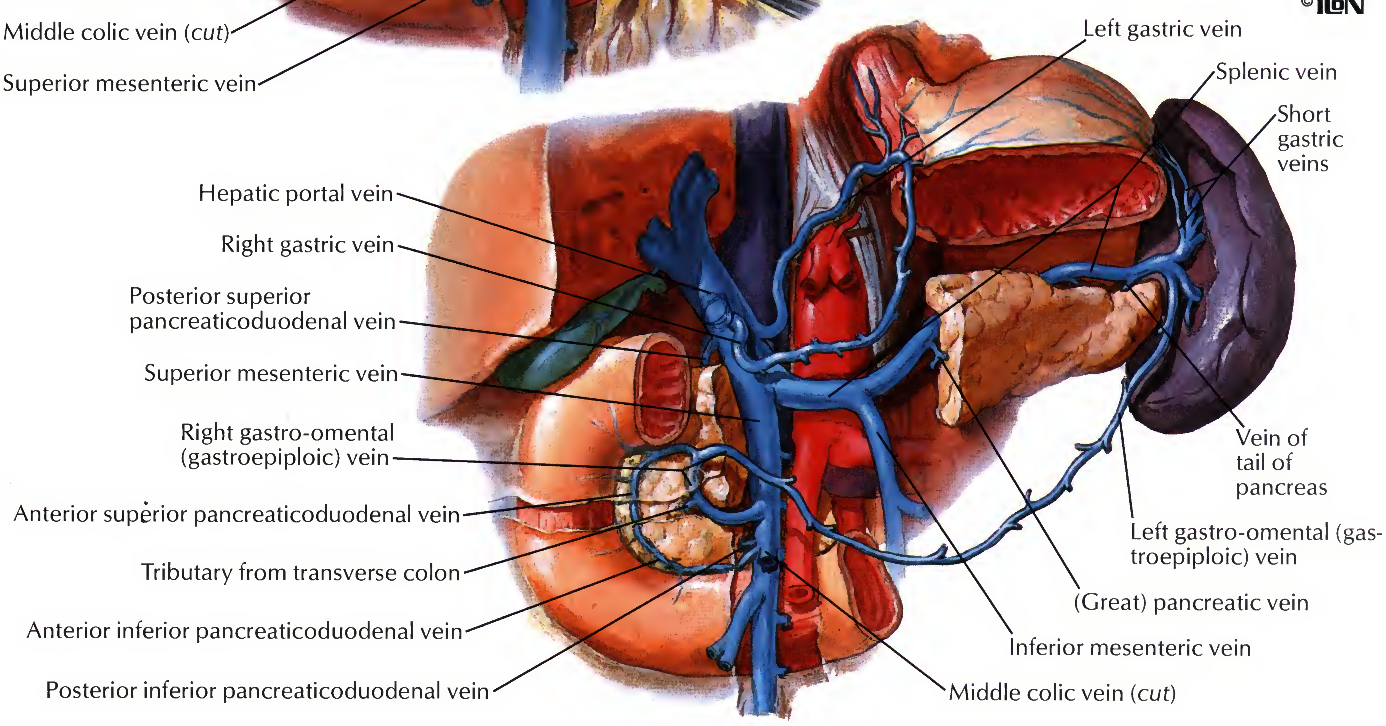
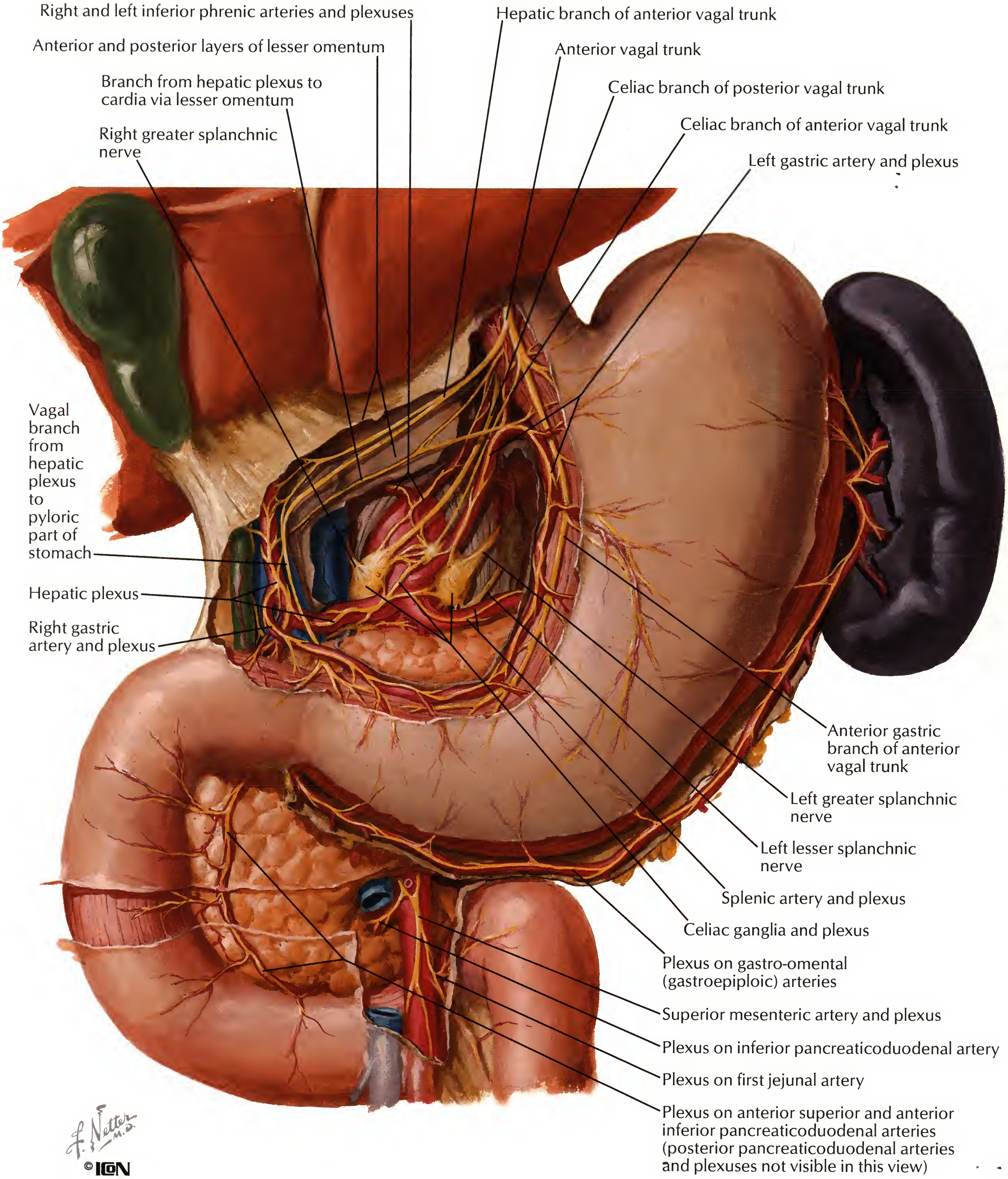
Veins of Stomach, Duodenum, Pancreas, and Spleen






Right and left inferior phrenic arteries and plexuses
Anterior and posterior layers of lesser omentum
Branch from hepatic plexus to cardia via lesser omentum
Right greater splanchnic nerve
Hepatic branch of anterior vagal trunk
Anterior vagal trunk
Celiac branch of posterior vagal trunk
Celiac branch of anterior vagal trunk
Left gastric artery and plexus
Vagal branch from hepatic plexus to pyloric part of stomach
Hepatic plexus
Right gastric artery and plexus
Anterior gastric branch of anterior vagal trunk
Left greater splanchnic nerve
Left lesser splanchnic nerve
Splenic artery and plexus
Celiac ganglia and plexus
Plexus on gastro-omental (gastroepiploic) arteries
Superior mesenteric artery and plexus
Plexus on inferior pancreaticoduodenal artery
Plexus on first jejunal artery
Plexus on anterior superior and anterior inferior pancreaticoduodenal arteries (posterior pancreaticoduodenal arteries and plexuses not visible in this view)
F. Netter M.D.
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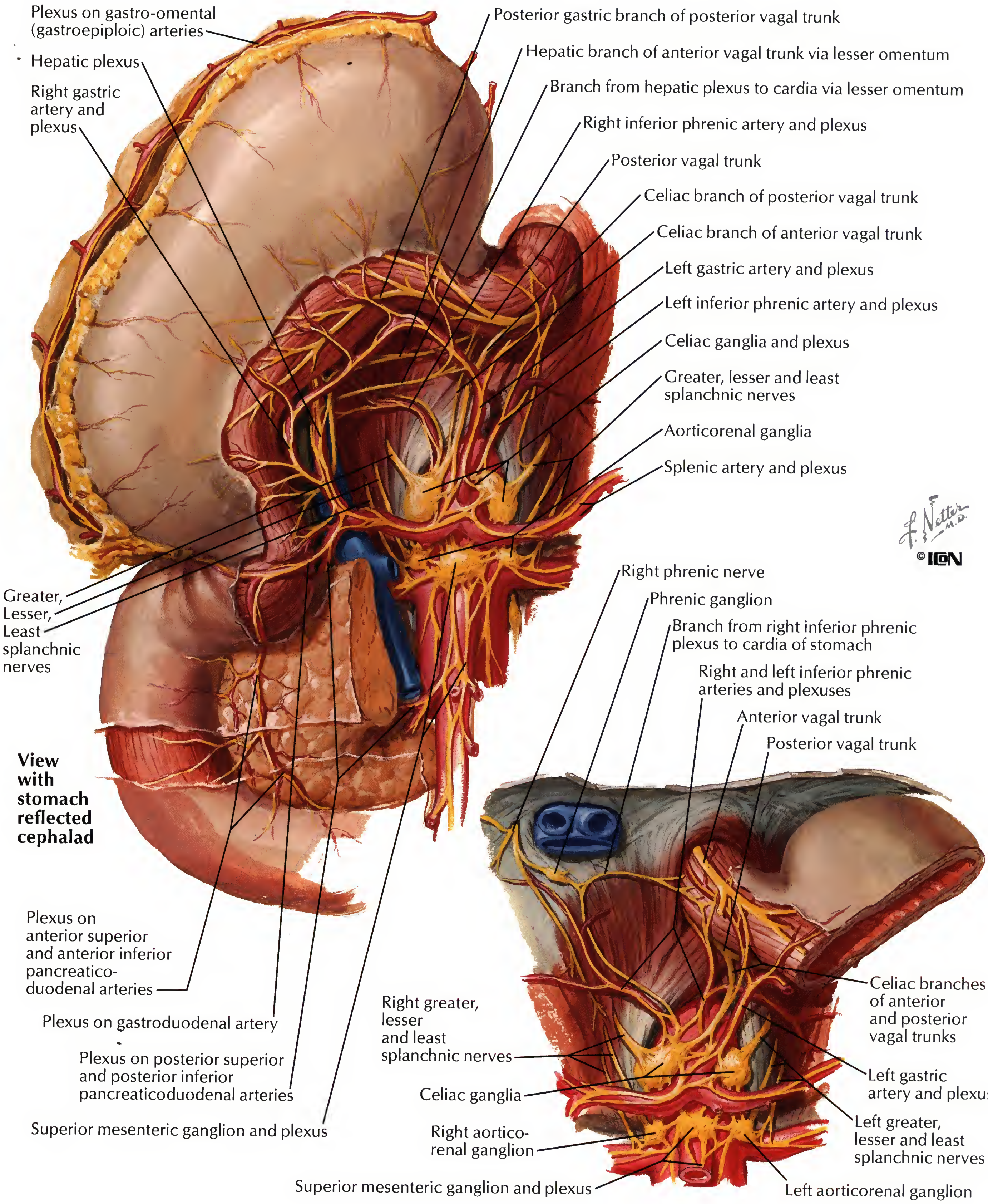
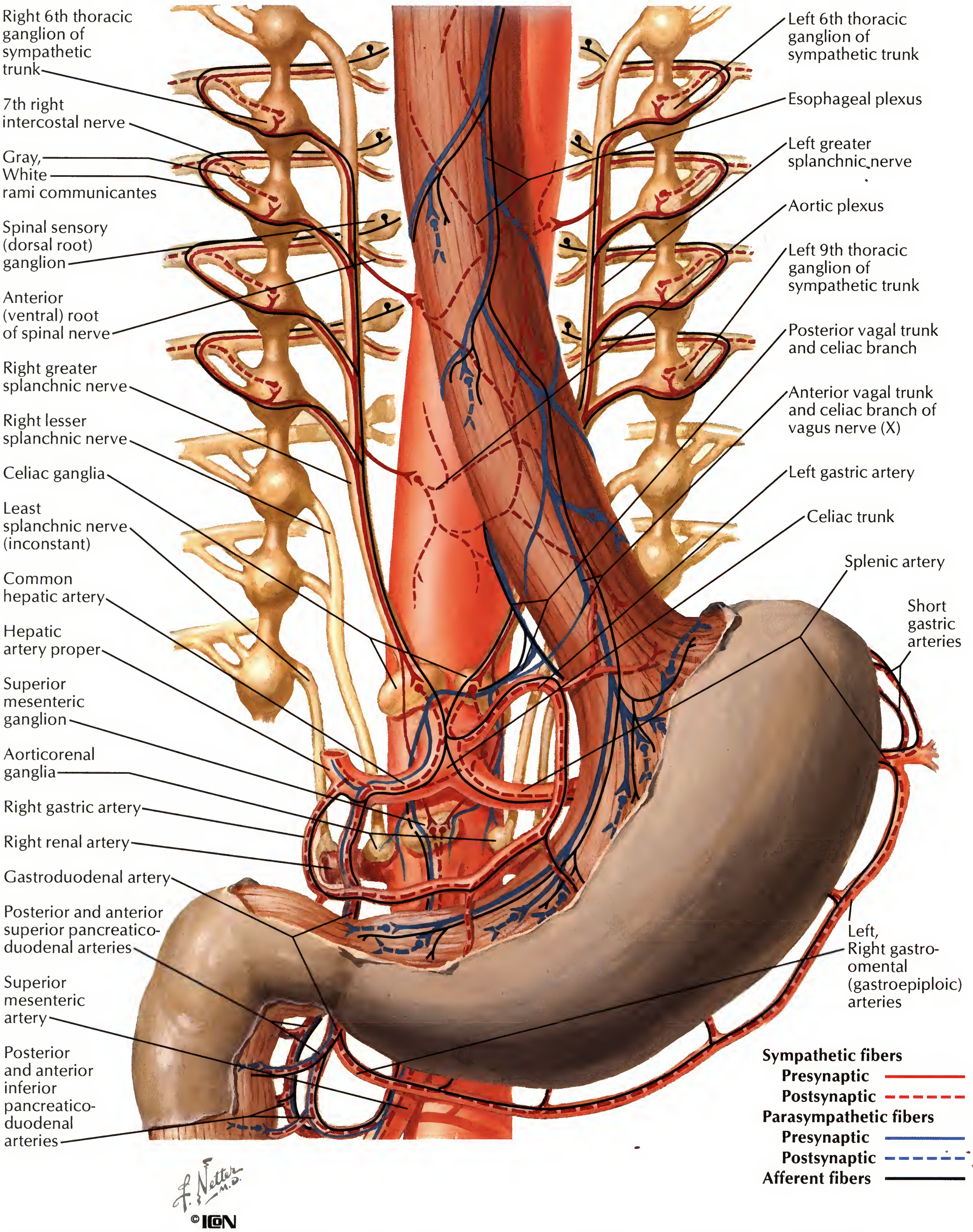


Plexus on gastro-omental (gastroepiploic) arteries
Hepatic plexus
Right gastric artery and plexus
Posterior gastric branch of posterior vagal trunk
Hepatic branch of anterior vagal trunk via lesser omentum
Branch from hepatic plexus to cardia via lesser omentum
Right inferior phrenic artery and plexus
Posterior vagal trunk
Celiac branch of posterior vagal trunk
Celiac branch of anterior vagal trunk
Left gastric artery and plexus
Left inferior phrenic artery and plexus
Celiac ganglia and plexus
Greater, lesser and least splanchnic nerves
Aorticorenal ganglia
Splenic artery and plexus
Greater, Lesser, Least splanchnic nerves
View with stomach reflected cephalad
Plexus on anterior superior and anterior inferior pancreatico-duodenal arteries
Plexus on gastroduodenal artery
Plexus on posterior superior and posterior inferior pancreaticoduodenal arteries
Superior mesenteric ganglion and plexus
F. Netter M.D.
©ICON
Right phrenic nerve
Phrenic ganglion
Branch from right inferior phrenic plexus to cardia of stomach
Right and left inferior phrenic arteries and plexuses
Anterior vagal trunk
Posterior vagal trunk
Celiac branches of anterior and posterior vagal trunks
Left gastric artery and plexus
Left greater, lesser and least splanchnic nerves
Left aorticorenal ganglion
Right greater, lesser and least splanchnic nerves
Celiac ganglia
Right aortico-renal ganglion
Superior mesenteric ganglion and plexus



Right 6th thoracic ganglion of sympathetic trunk
7th right intercostal nerve
Gray,
White
rami communicantes
Spinal sensory (dorsal root) ganglion
Anterior (ventral) root of spinal nerve
Right greater splanchnic nerve
Right lesser splanchnic nerve
Celiac ganglia
Least splanchnic nerve (inconstant)
Common hepatic artery
Hepatic artery proper
Superior mesenteric ganglion
Aorticorenal ganglia
Right gastric artery
Right renal artery
Gastroduodenal artery
Posterior and anterior superior pancreaticoduodenal arteries
Superior mesenteric artery
Posterior and anterior inferior pancreaticoduodenal arteries
Left 6th thoracic ganglion of sympathetic trunk
Esophageal plexus
Left greater splanchnic nerve
Aortic plexus
Left 9th thoracic ganglion of sympathetic trunk
Posterior vagal trunk and celiac branch
Anterior vagal trunk and celiac branch of vagus nerve (X)
Left gastric artery
Celiac trunk
Splenic artery
Short gastric arteries
Left,
Right gastro-omental (gastroepiploic) arteries
Sympathetic fibers
Presynaptic
Postsynaptic
Parasympathetic fibers
Presynaptic
Postsynaptic
Afferent fibers
F. Netter M.D.
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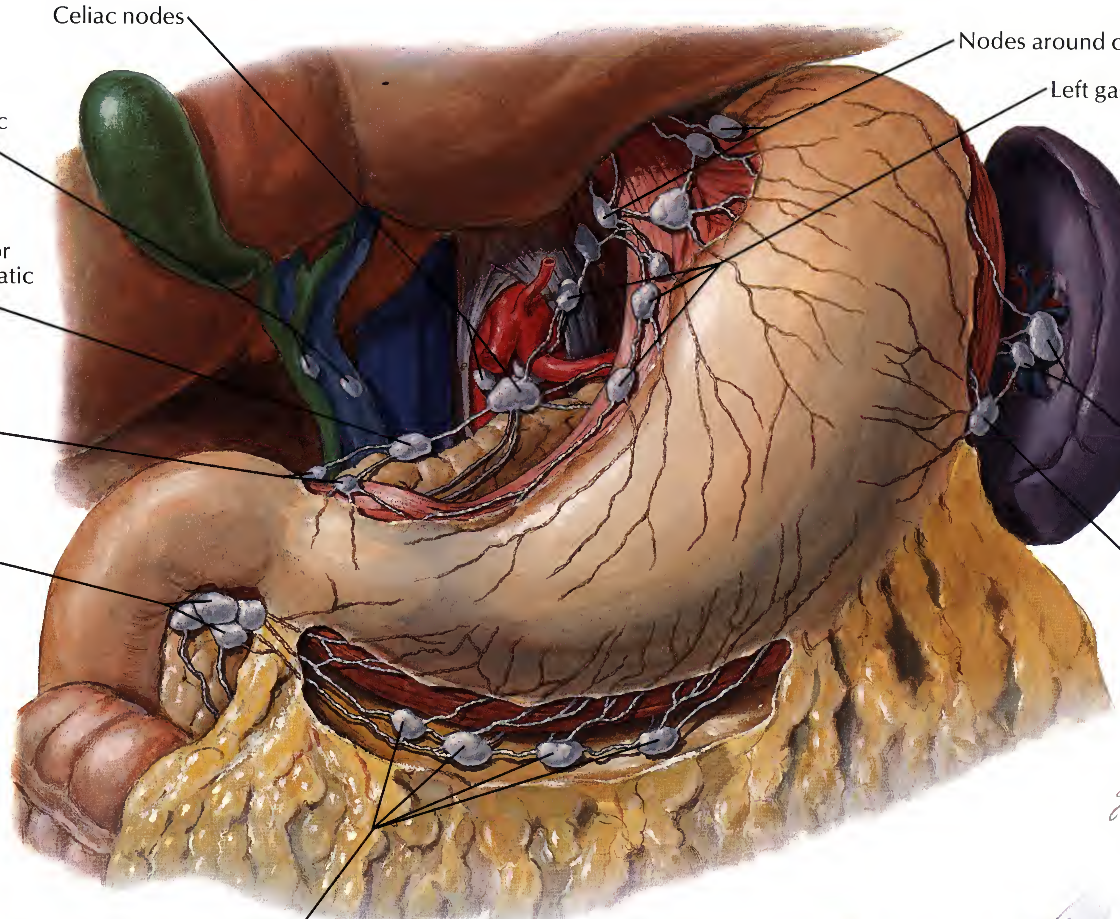
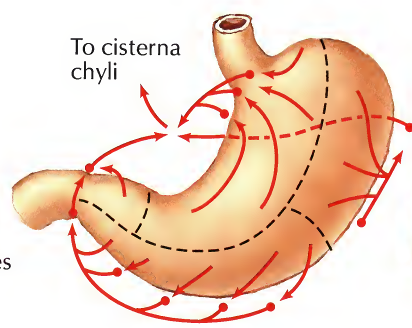
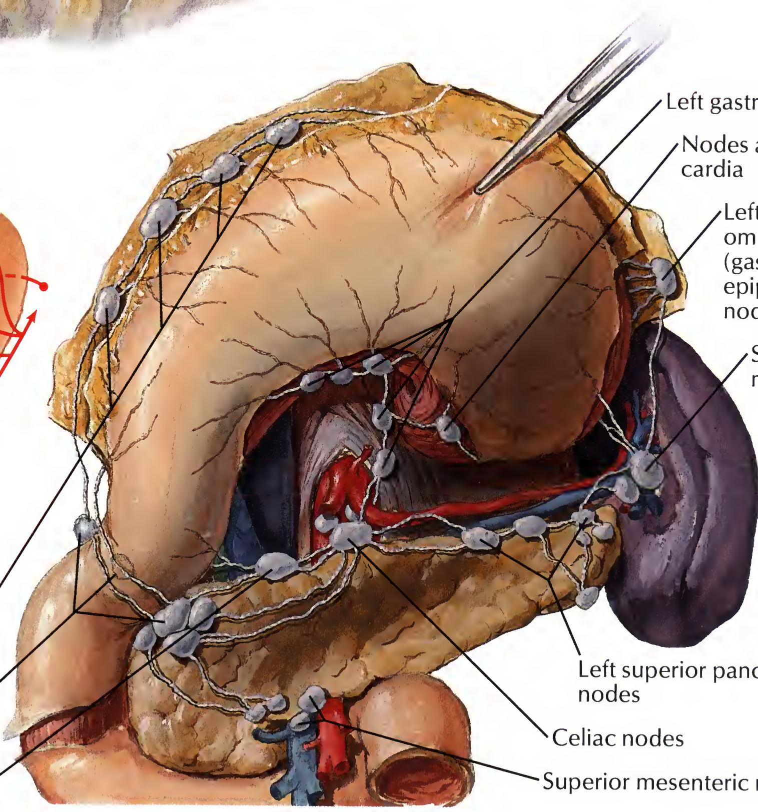
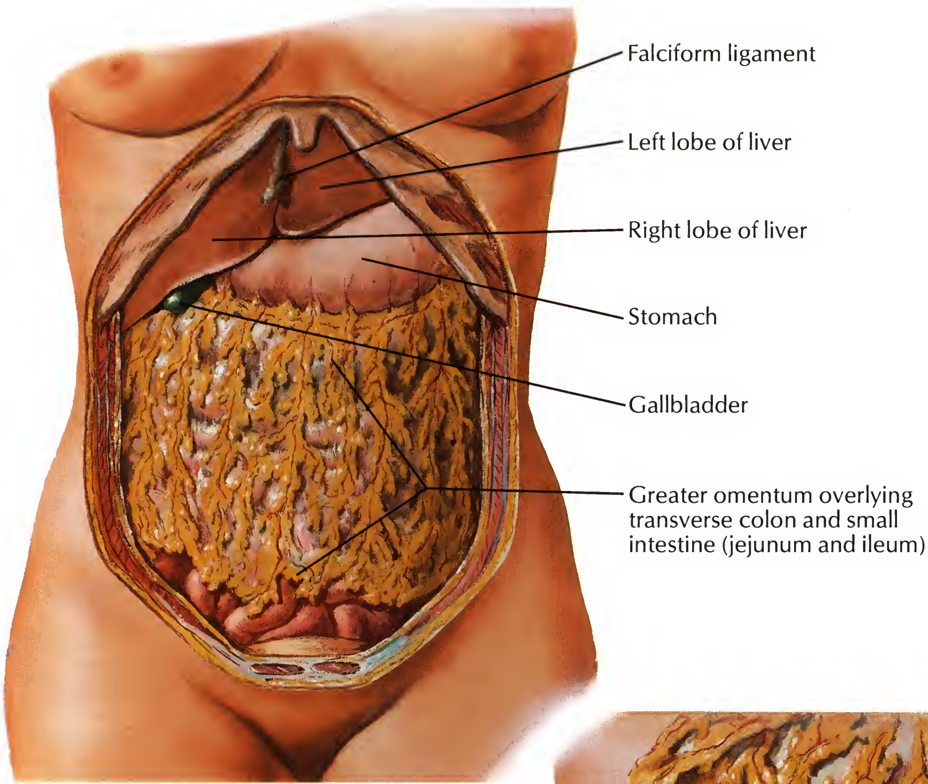
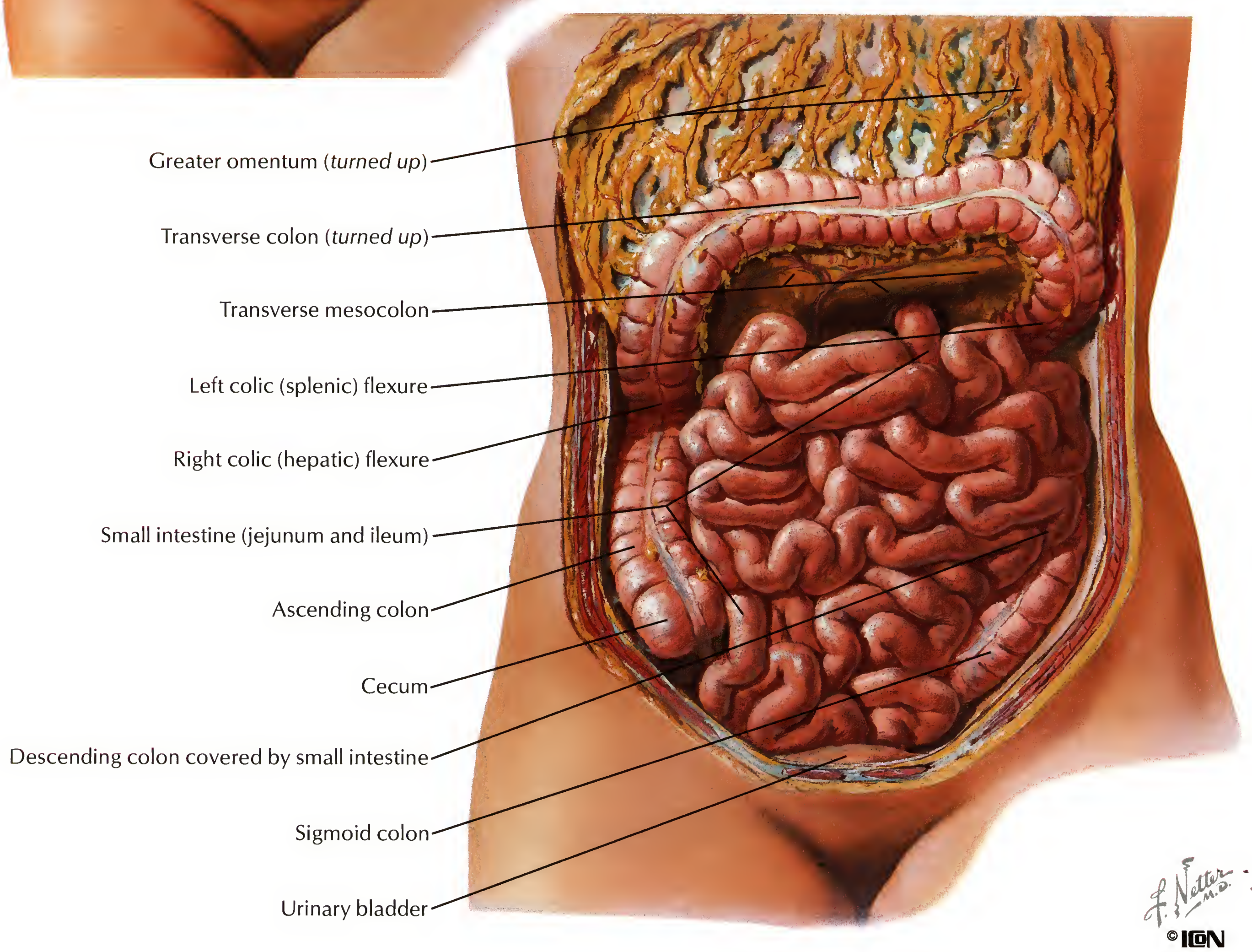
Lymph Vessels and Nodes of Stomach








Falciform ligament
Left lobe of liver
Right lobe of liver
Stomach
Gallbladder
Greater omentum overlying transverse colon and small intestine (jejunum and ileum)


Greater omentum (*turned up*)
Transverse colon (*turned up*)
Transverse mesocolon
Left colic (splenic) flexure
Right colic (hepatic) flexure
Small intestine (jejunum and ileum)
Ascending colon
Cecum
Descending colon covered by small intestine
Sigmoid colon
Urinary bladder
F. Netter M.D.
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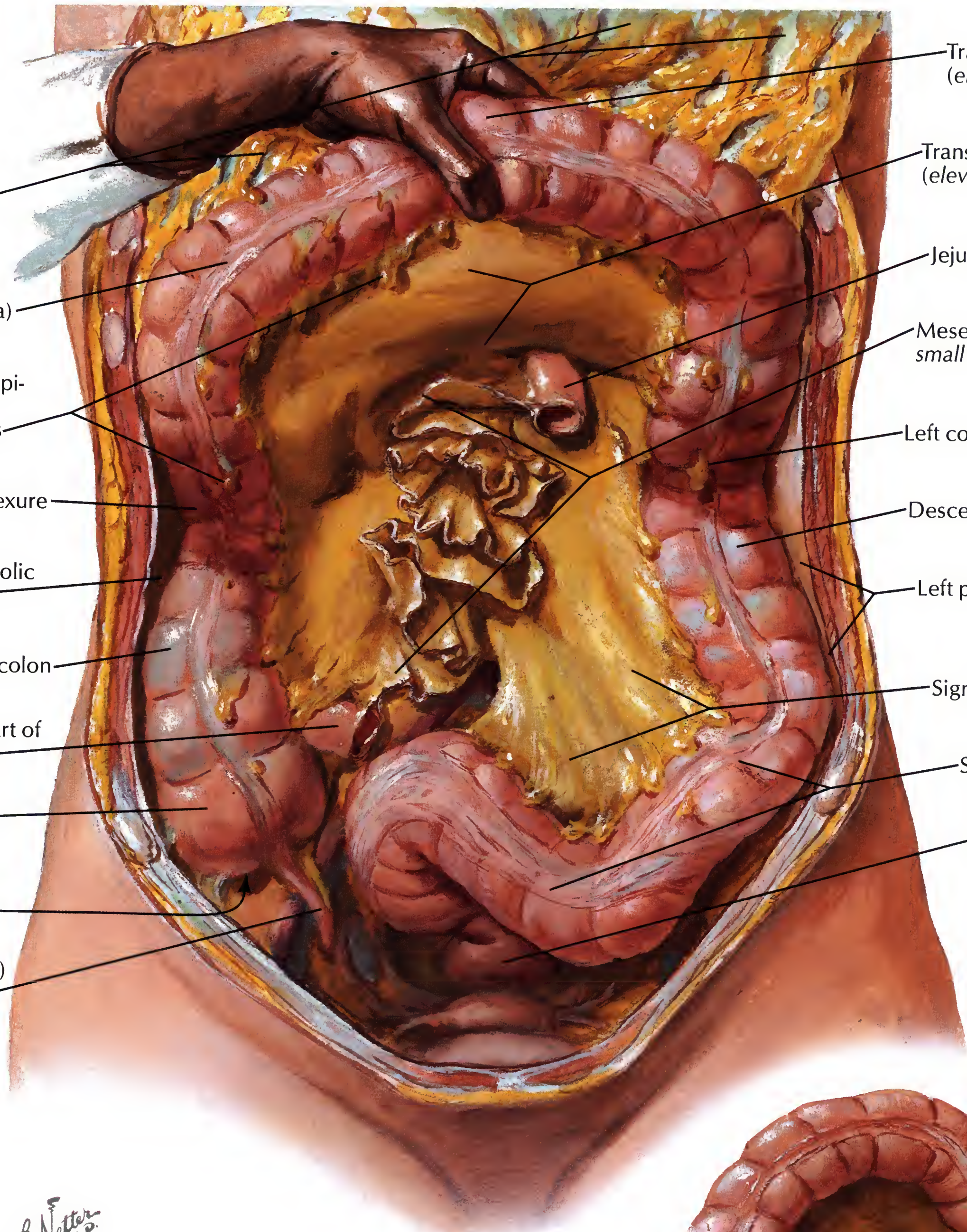
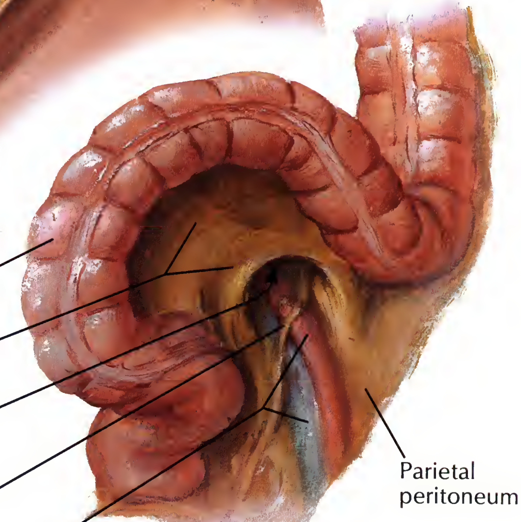
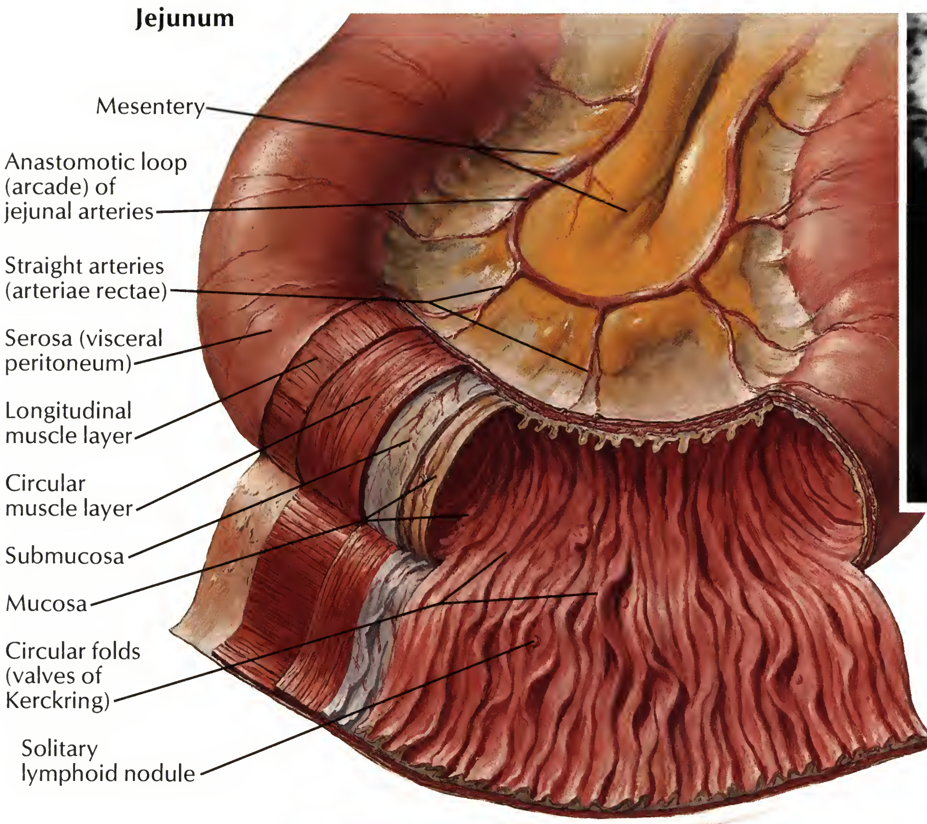
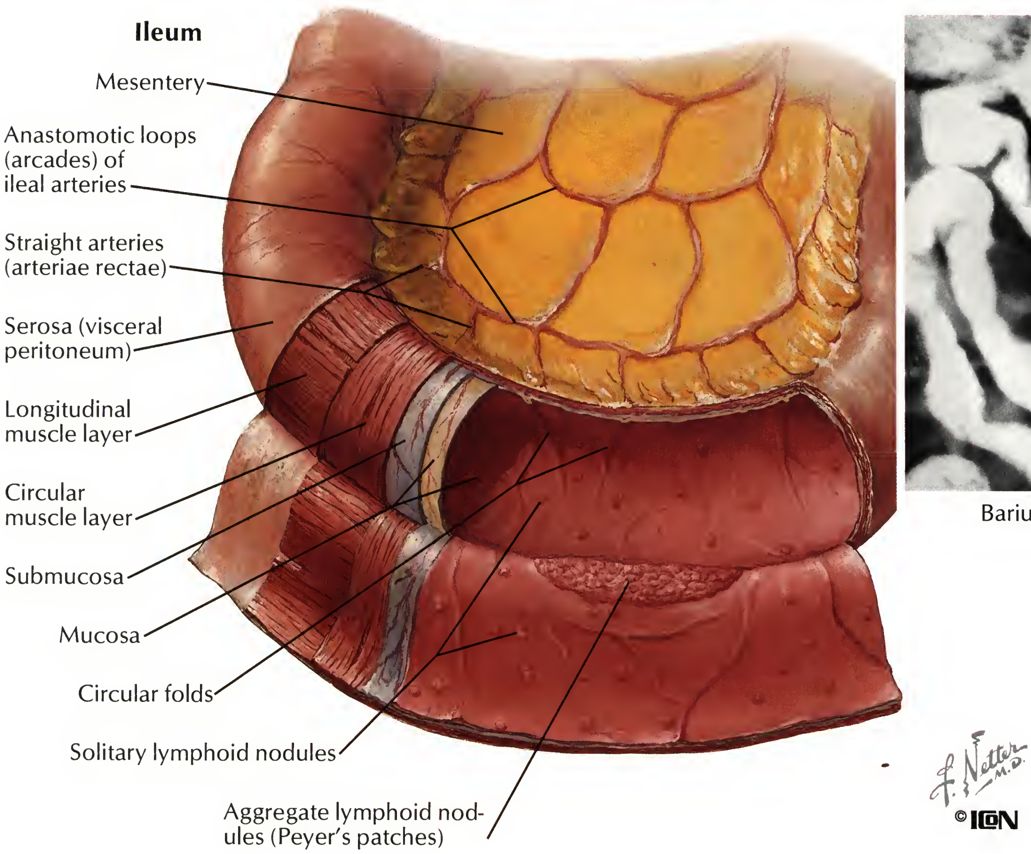
Mesenteric Relations of Intestines







Barium radiograph of jejunum



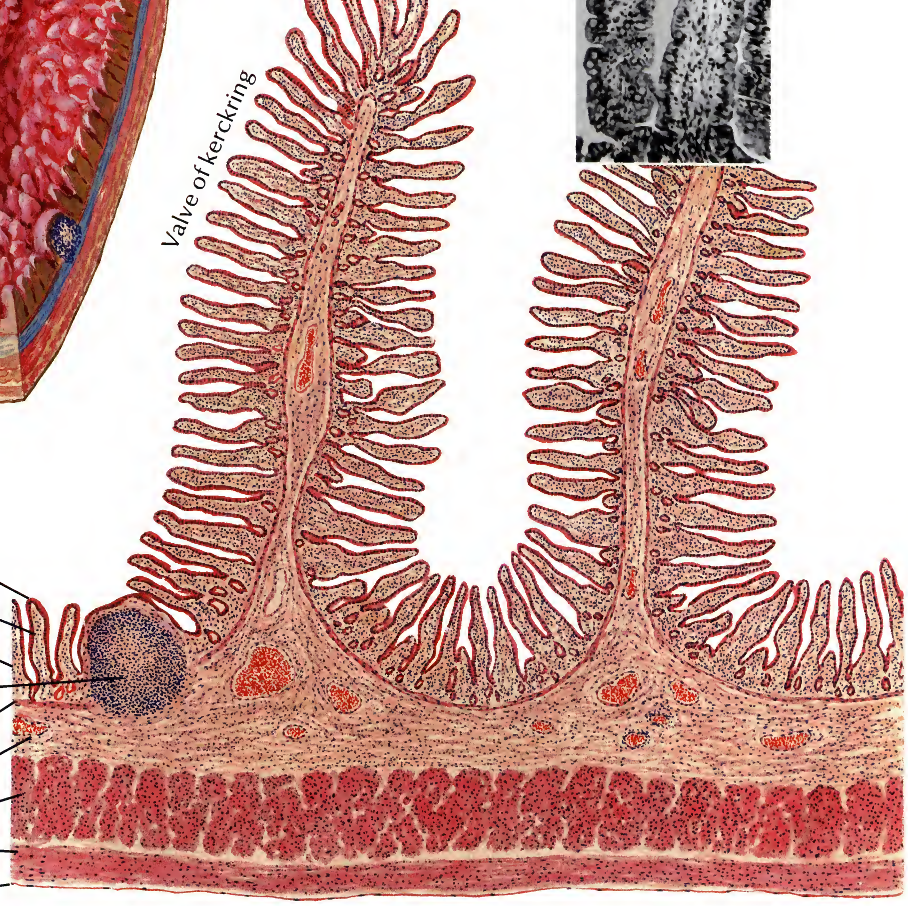
Barium radiograph of ileum

Structure of Small Intestine

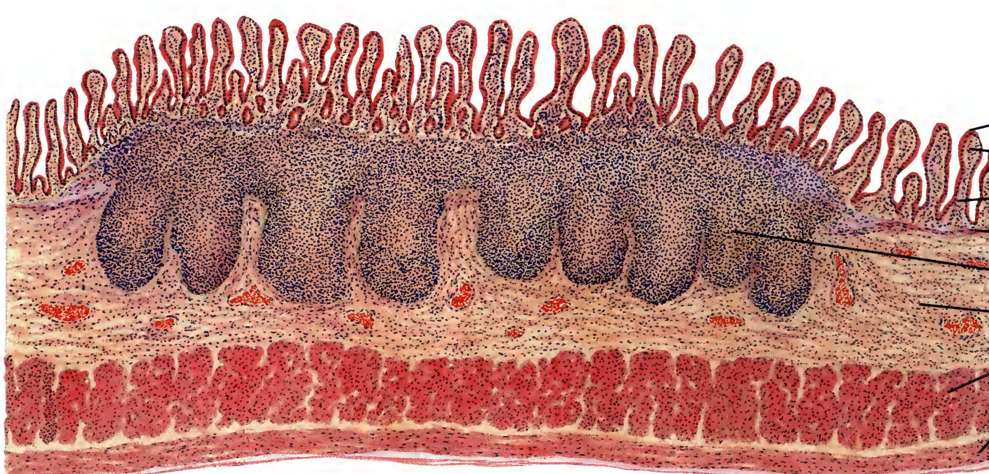
Three-dimensional magnification of jejunal wall

Two jejunal villi (x 100); (left in contraction, right relaxed)

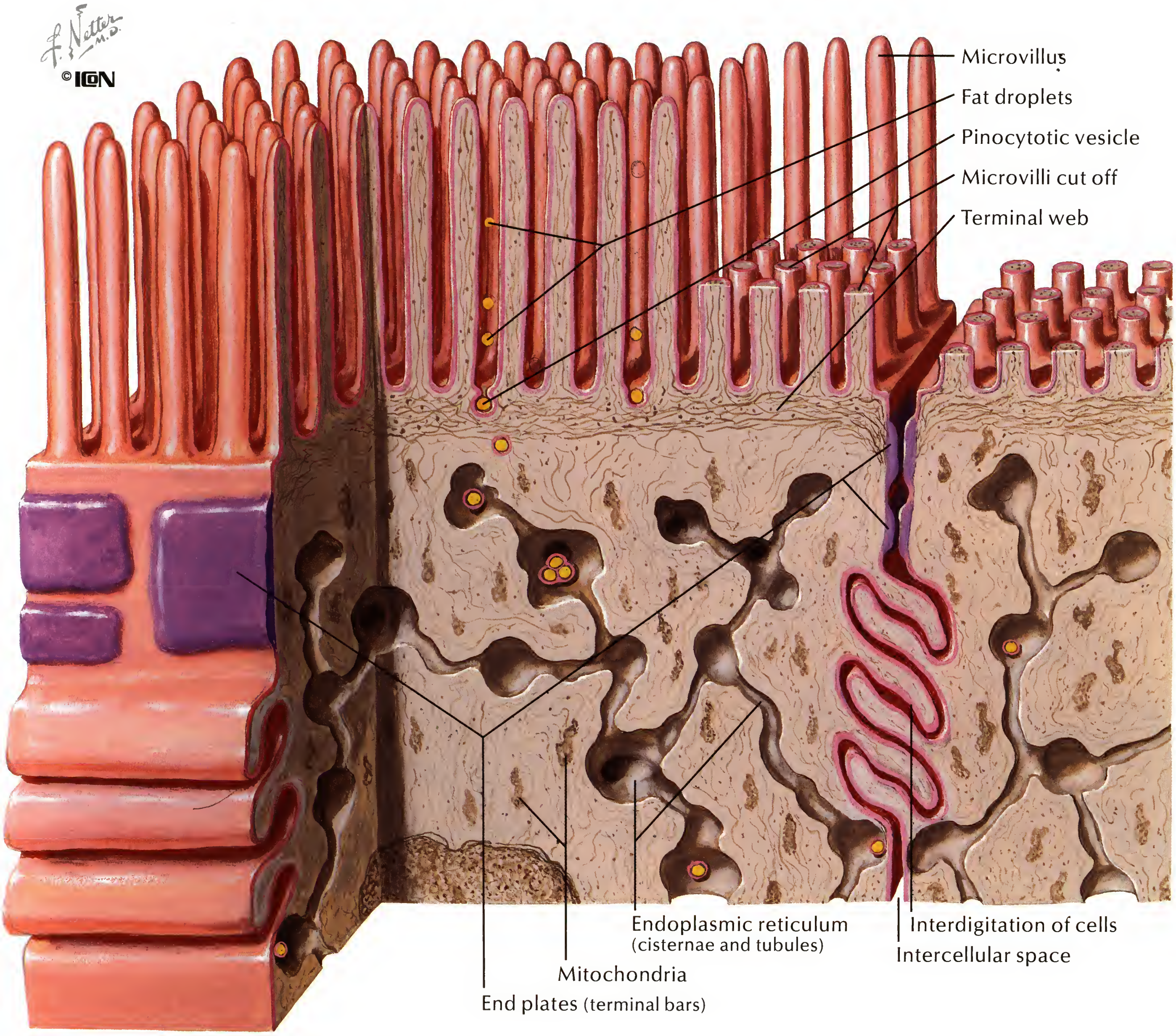
Jejunum (high power)



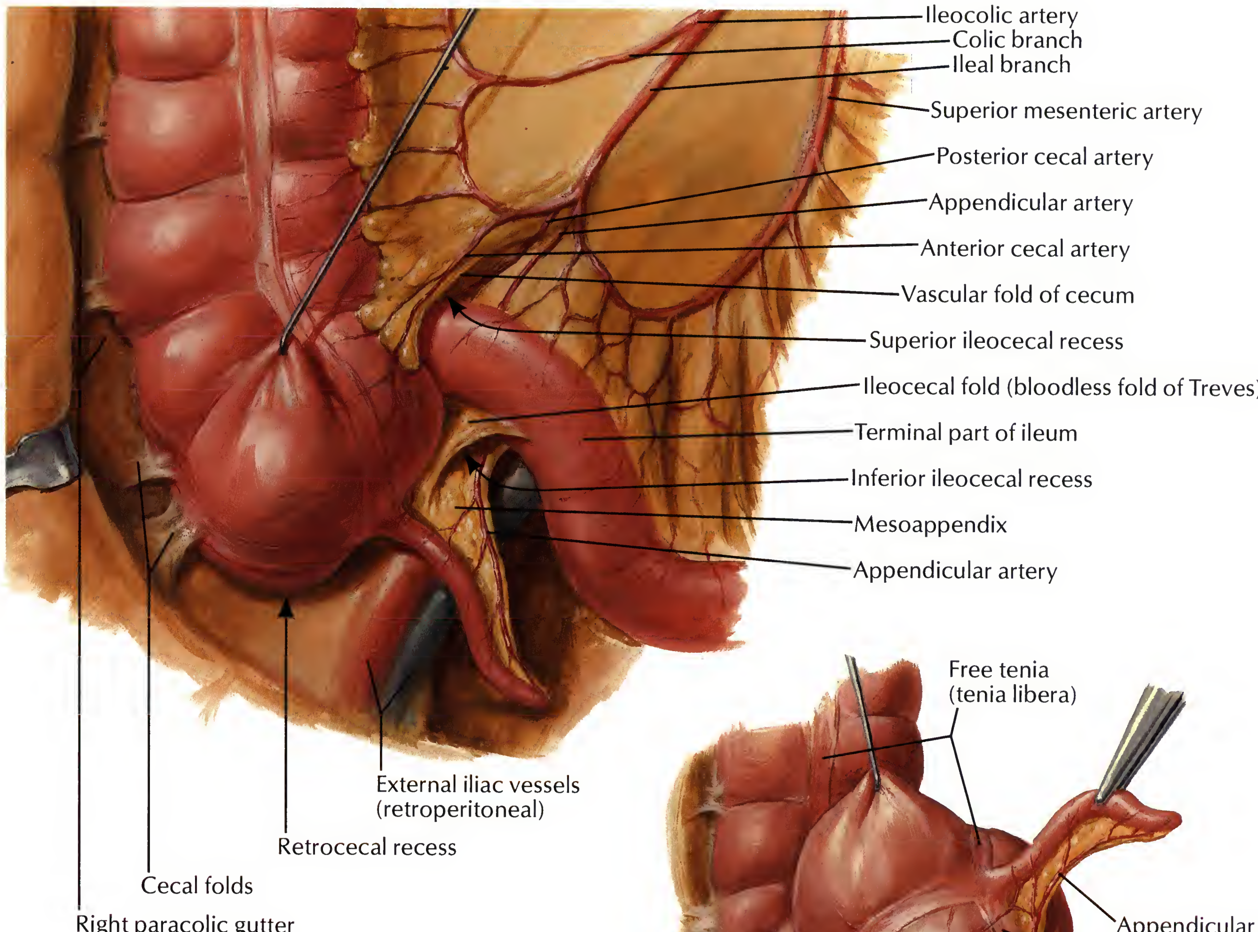
Jejunum (low power)

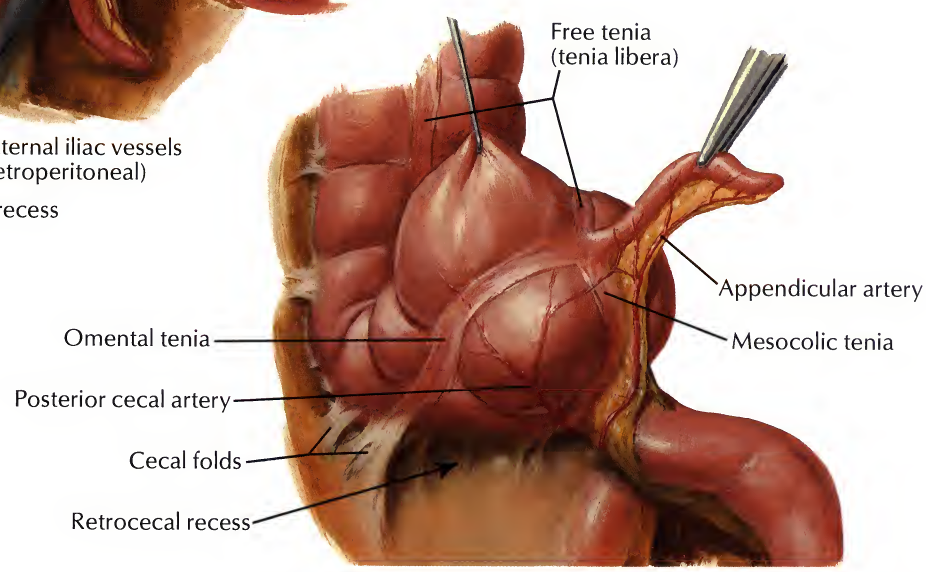


Ileum (low power)

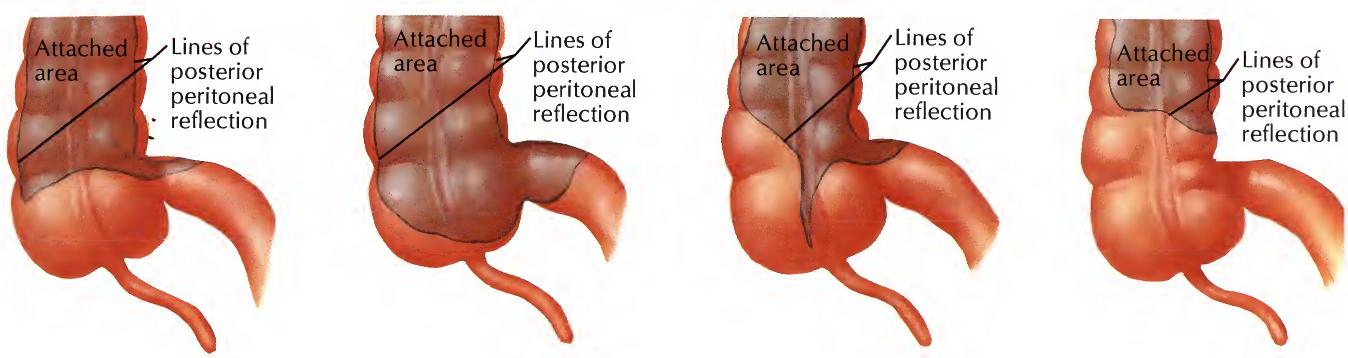


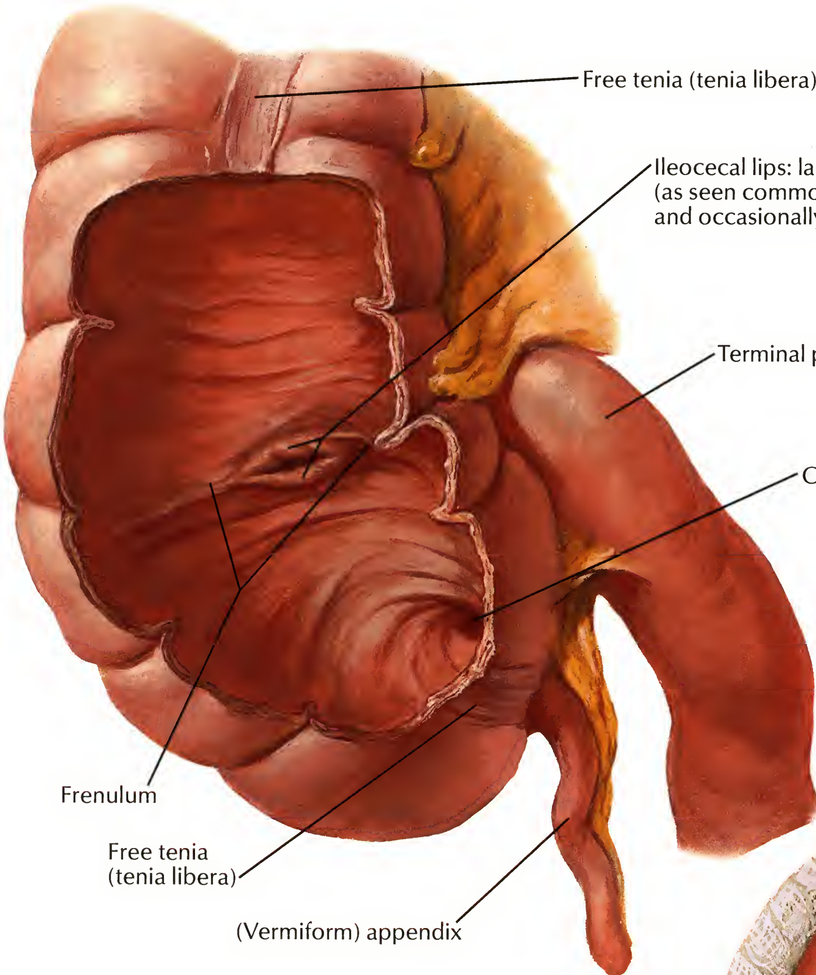
Three-dimensional schema of striated border of intestinal epithelial cells (based on ultramicroscopic studies)

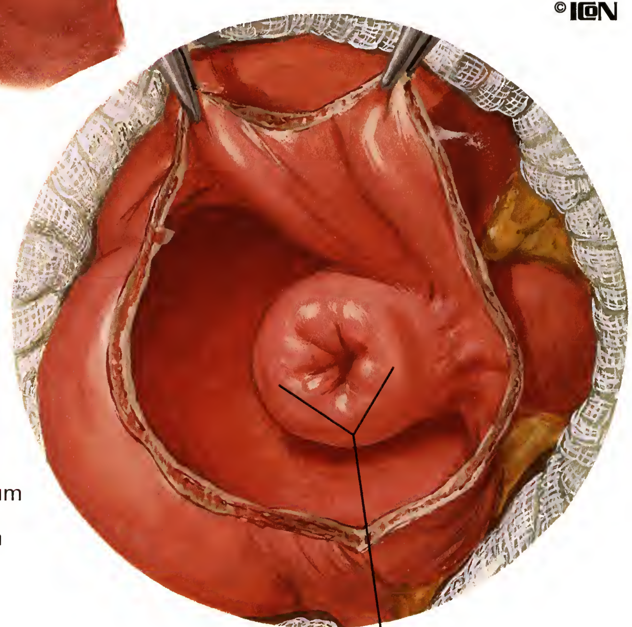


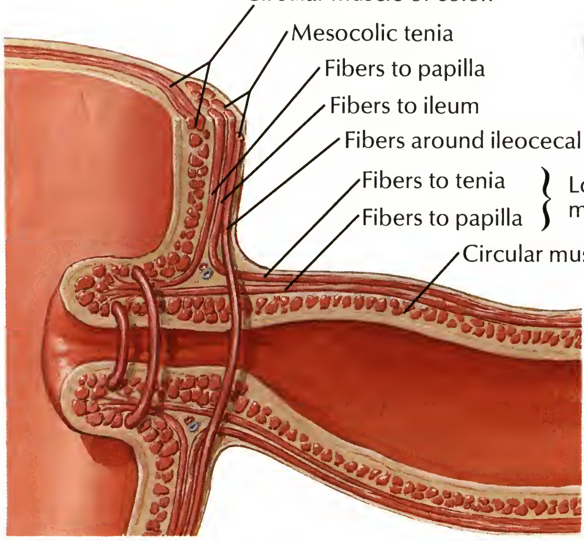


Some variations in posterior peritoneal attachment of cecum



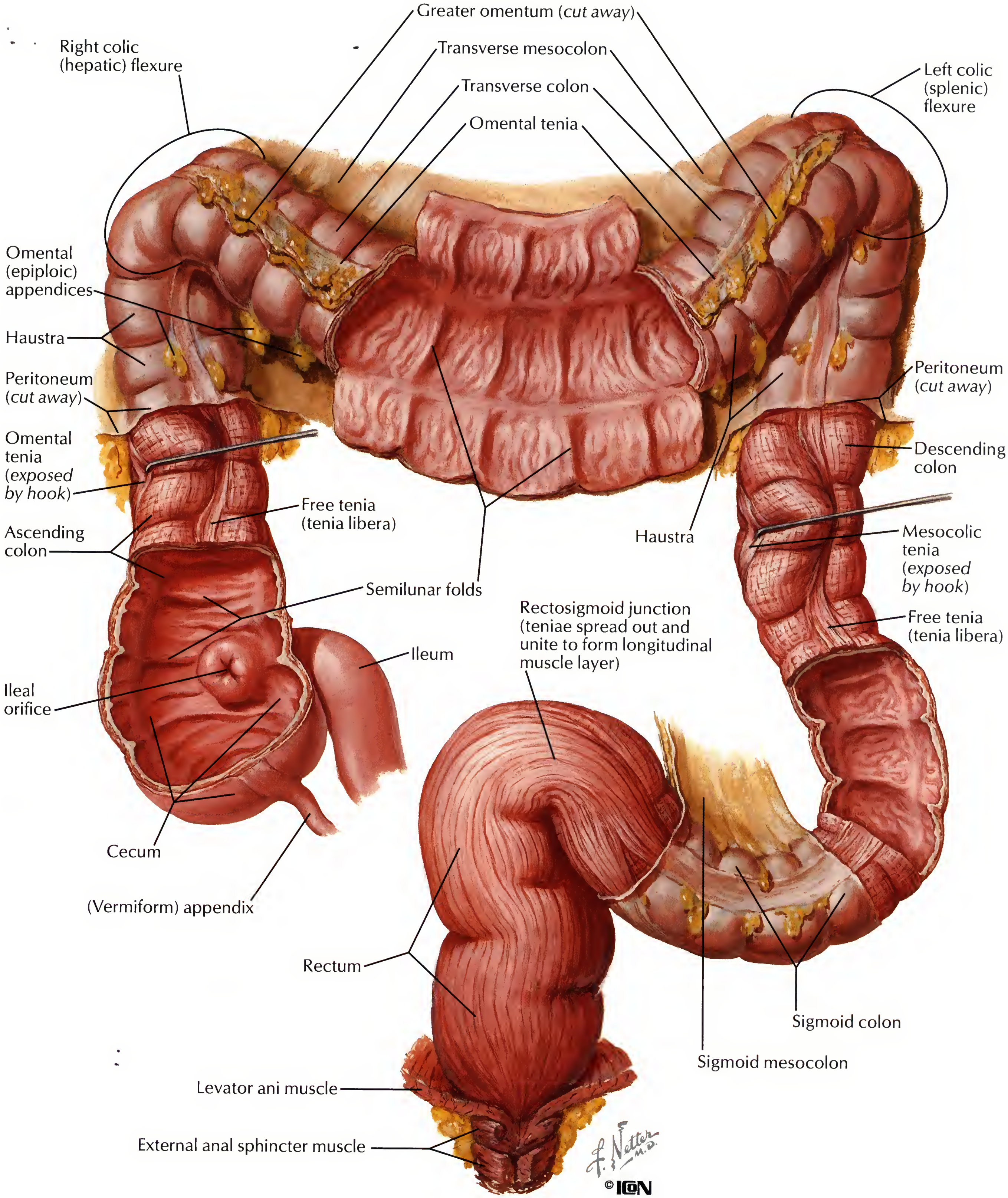


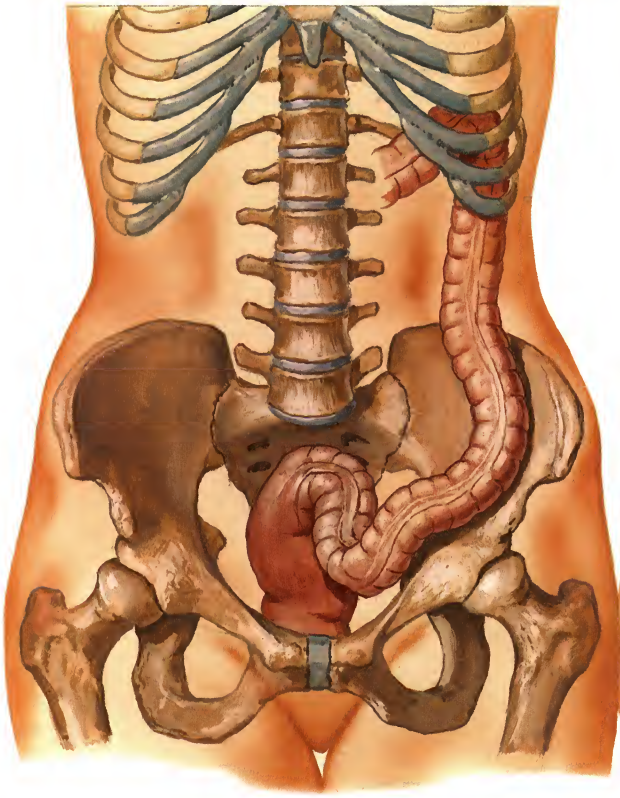




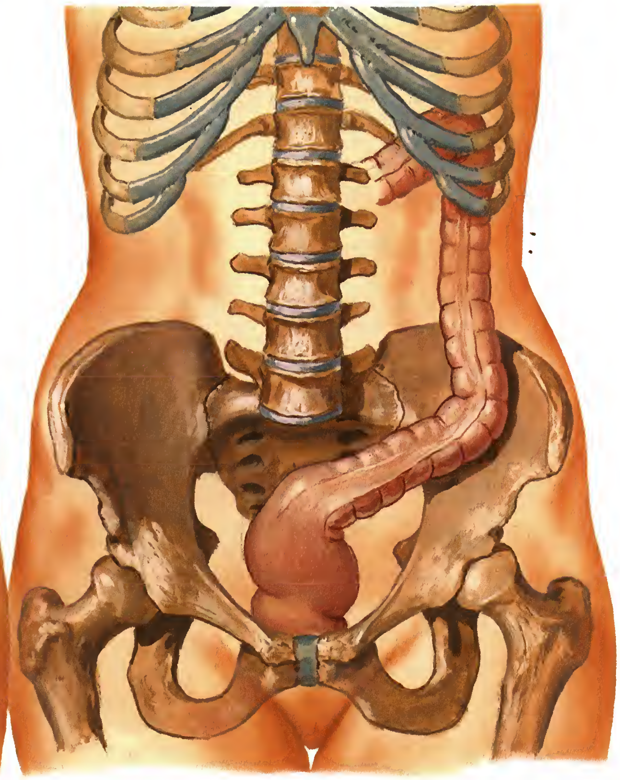
Schema of muscle fibers at ileal orifice

Mucosa and Musculature of Colon

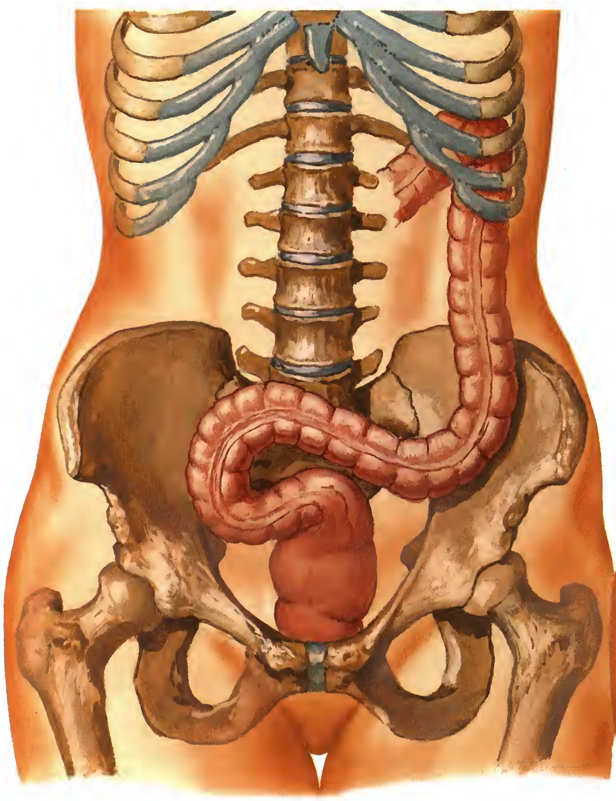




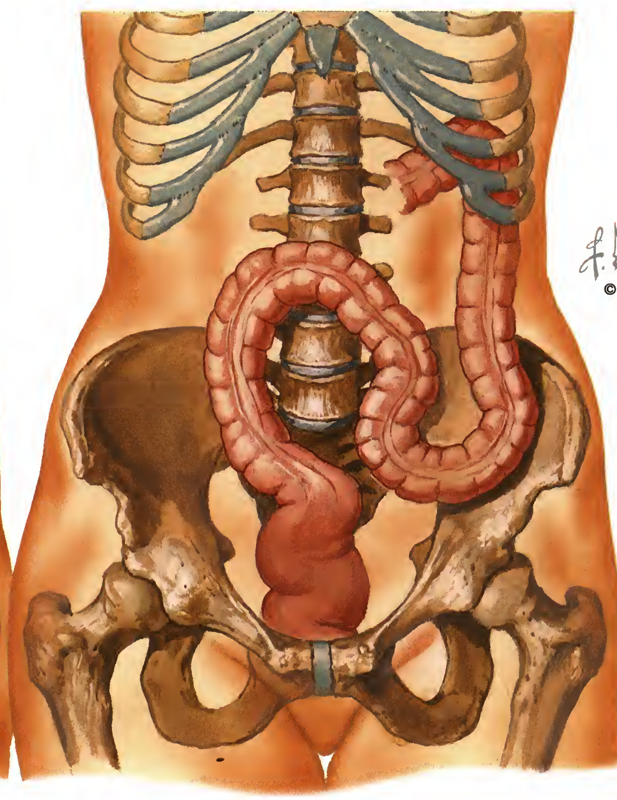
Typical



Short, straight, obliquely into pelvis

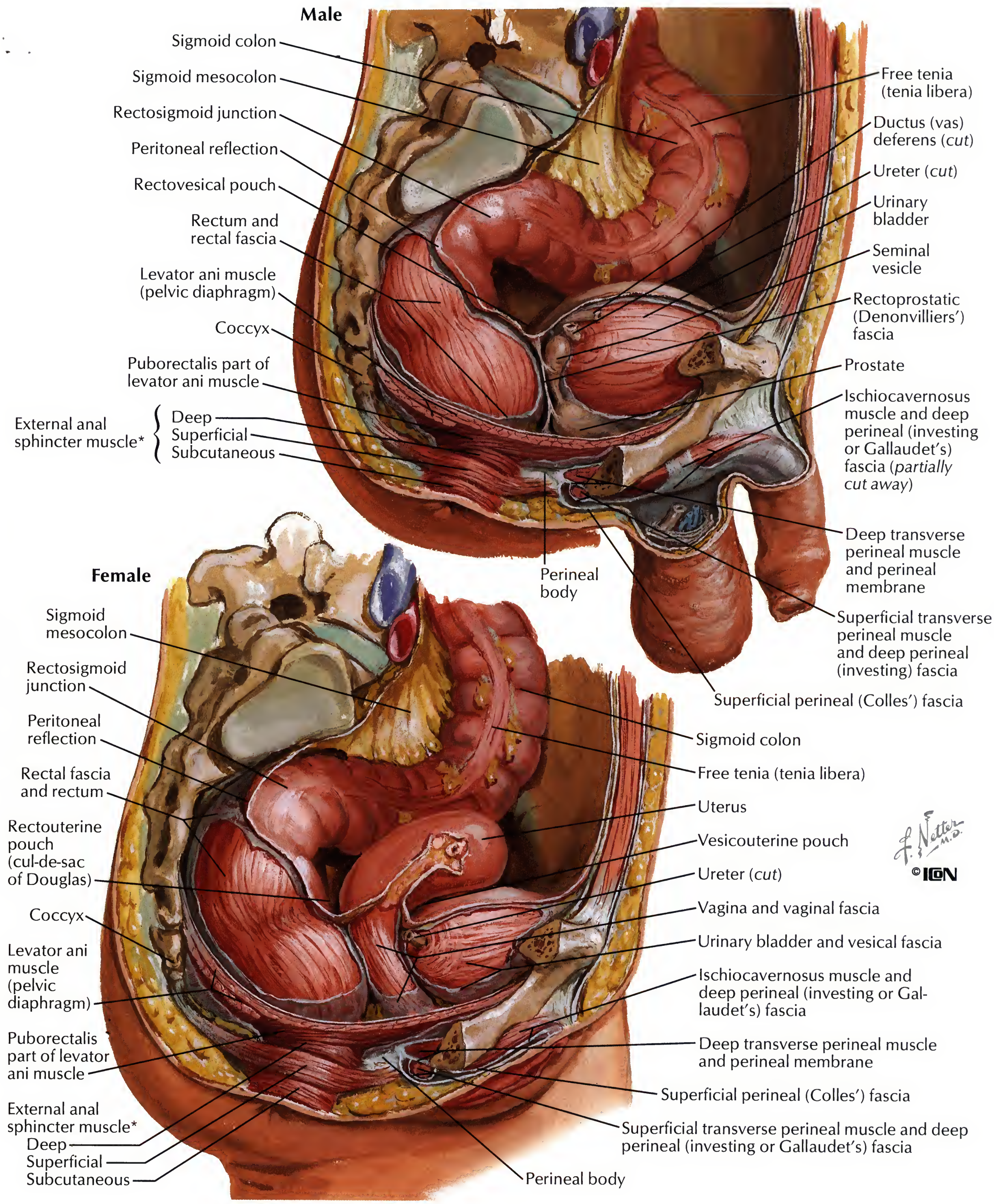


Looping to right side

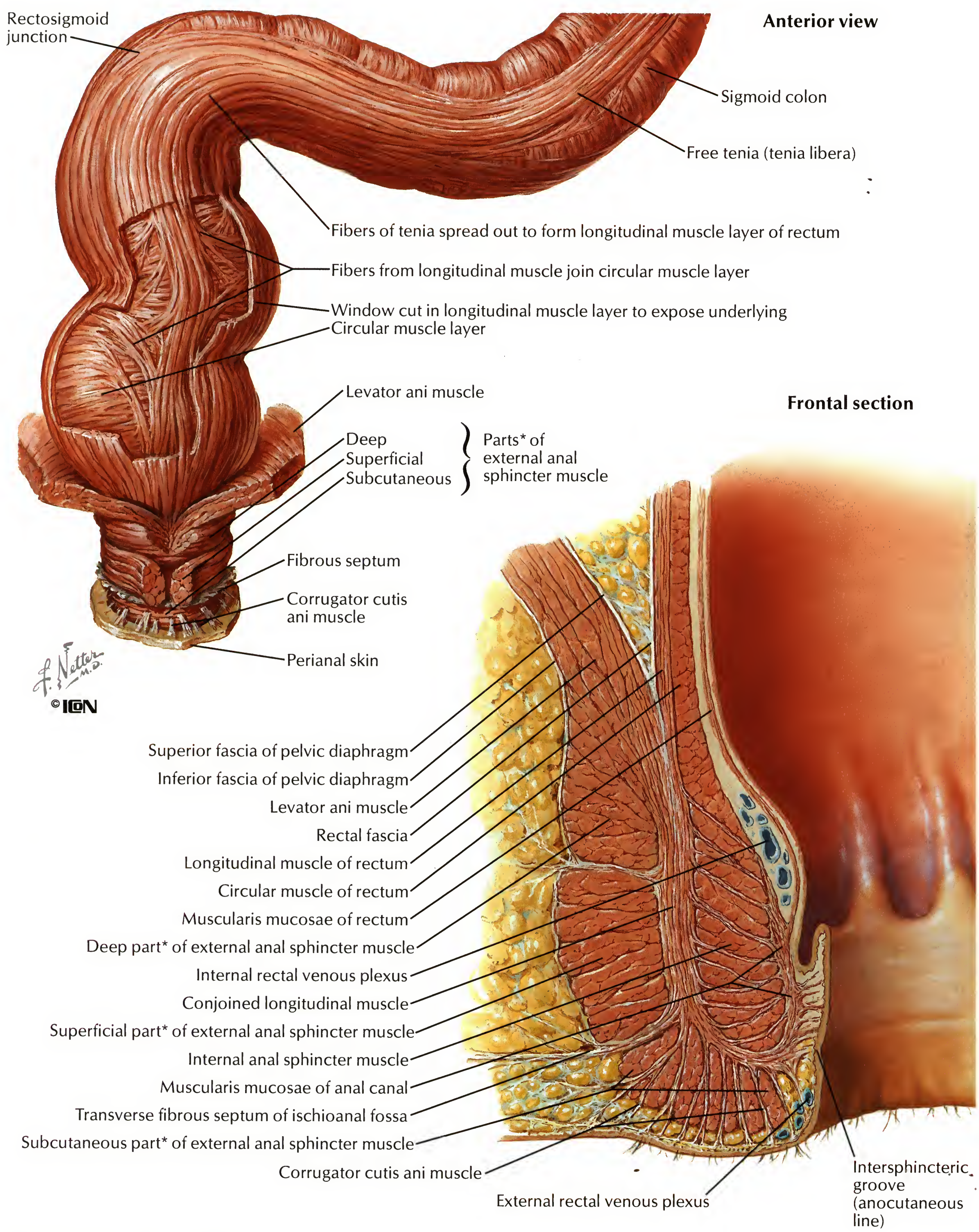


Ascending high into abdomen

Rectum in Situ: Male and Female

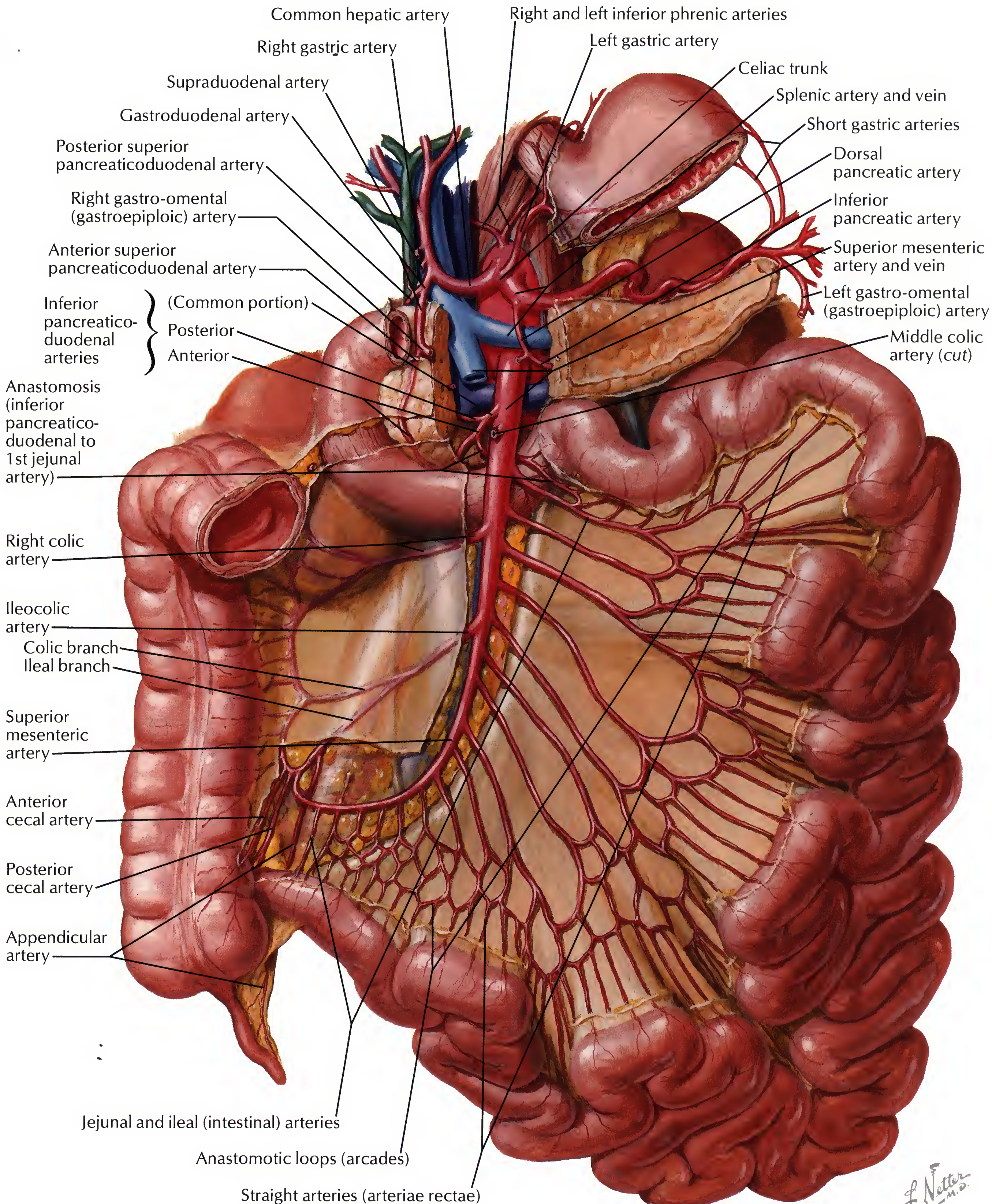


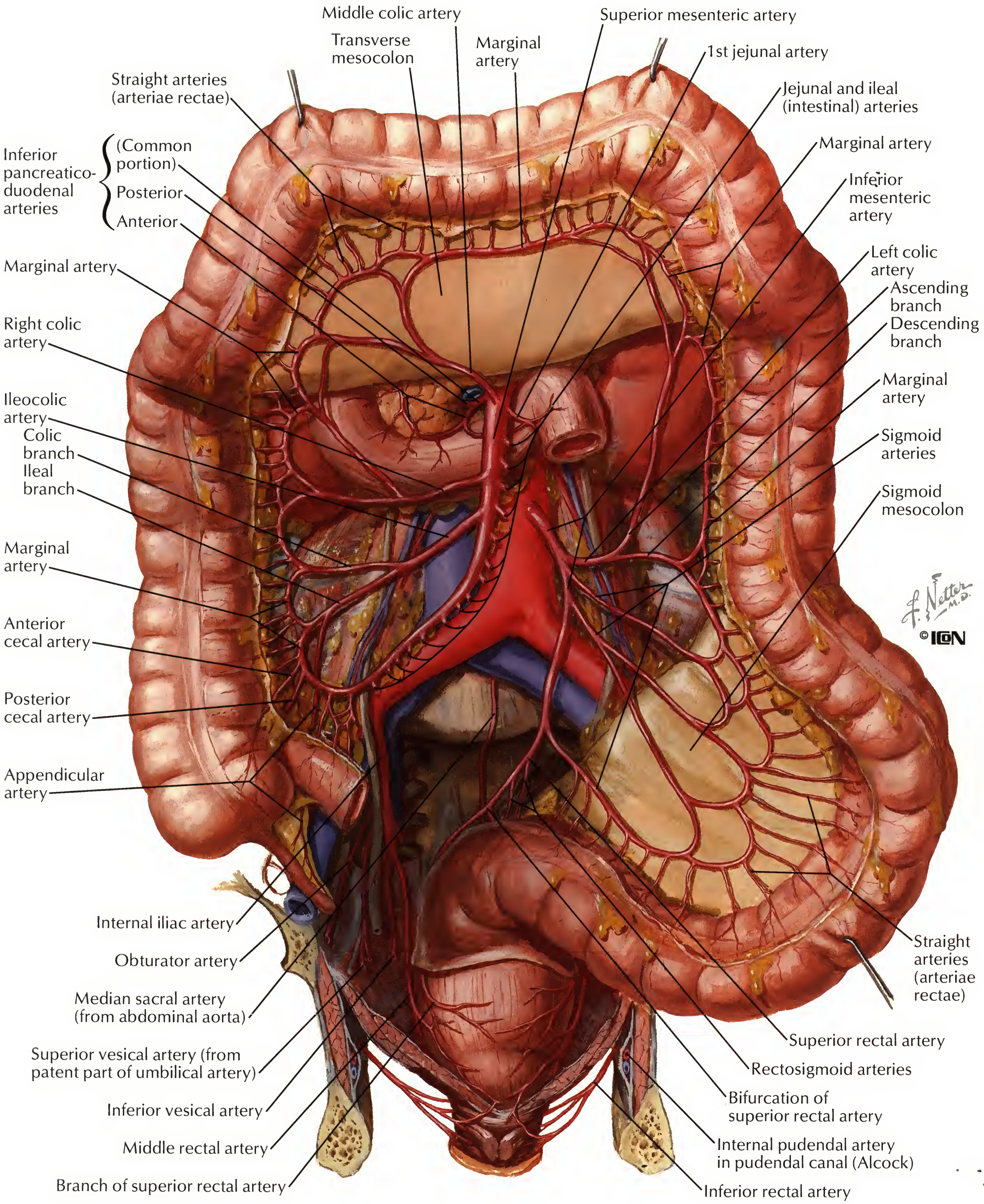
*Parts variable and often indistinct



*Parts variable and often indistinct

Arteries of Small Intestine




Middle colic artery
Transverse mesocolon
Marginal artery
Superior mesenteric artery
1st jejunal artery
Straight arteries (arteriae rectae)
Jejunal and ileal (intestinal) arteries
Marginal artery
Inferior pancreaticoduodenal arteries
(Common portion)
Posterior
Anterior
Inferior mesenteric artery
Left colic artery
Ascending branch
Descending branch
Marginal artery
Right colic artery
Marginal artery
Ileocolic artery
Colic branch
Ileal branch
Sigmoid arteries
Sigmoid mesocolon
Marginal artery
Anterior cecal artery
Posterior cecal artery
Appendicular artery
Internal iliac artery
Obturator artery
Median sacral artery (from abdominal aorta)
Superior vesical artery (from patent part of umbilical artery)
Inferior vesical artery
Middle rectal artery
Branch of superior rectal artery
Straight arteries (arteriae rectae)
Superior rectal artery
Rectosigmoid arteries
Bifurcation of superior rectal artery
Internal pudendal artery in pudendal canal (Alcock)
Inferior rectal artery
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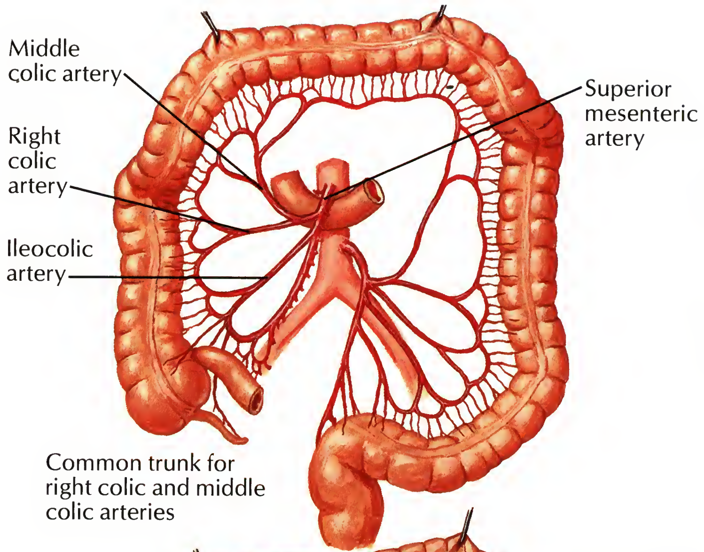
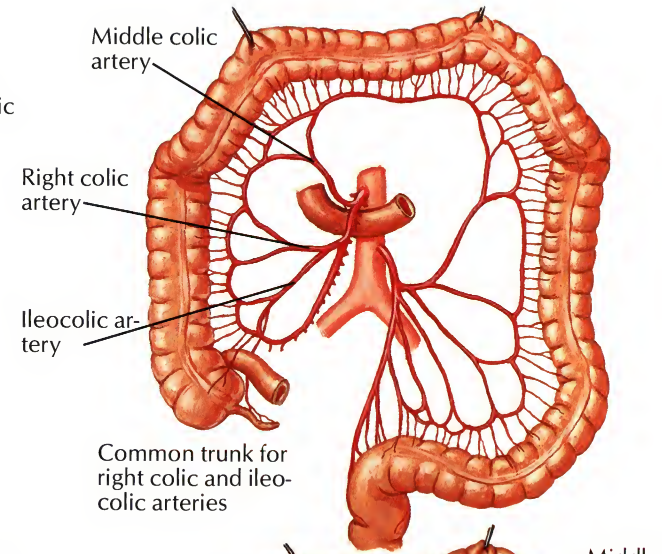
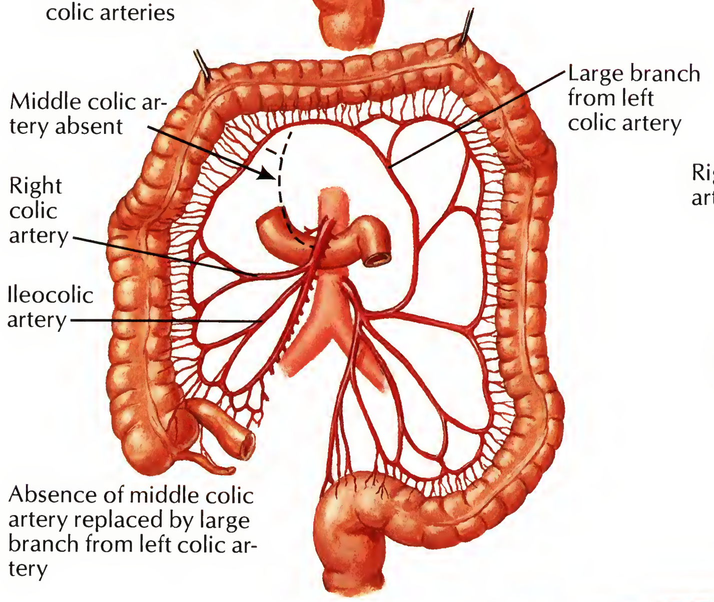
Variations in Colic Arteries



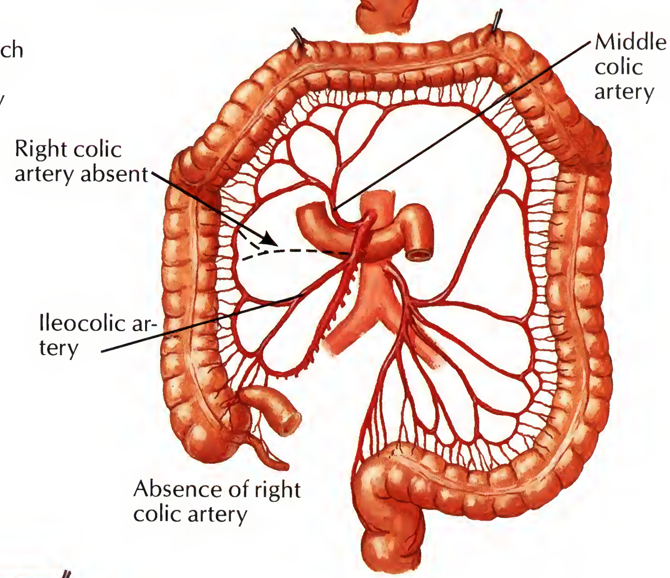
Common trunk for right colic and middle colic arteries



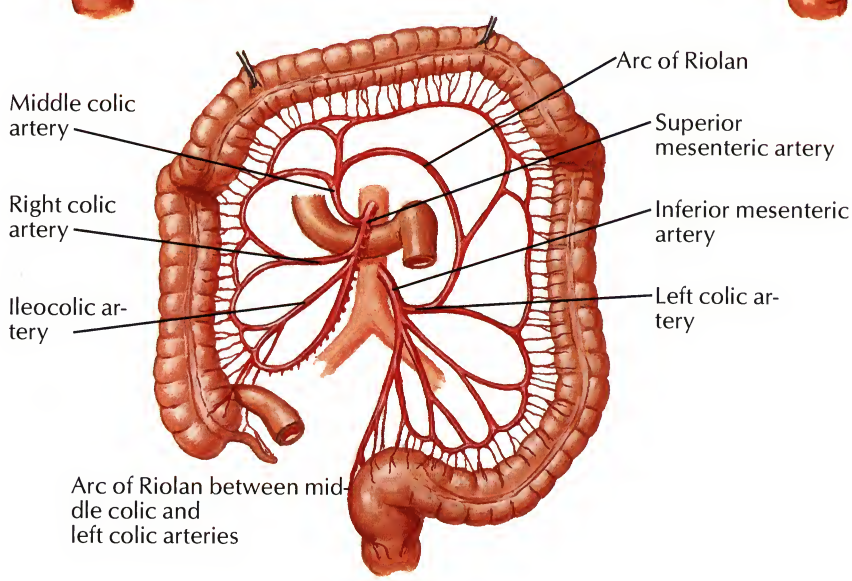
Common trunk for right colic and ileocolic arteries



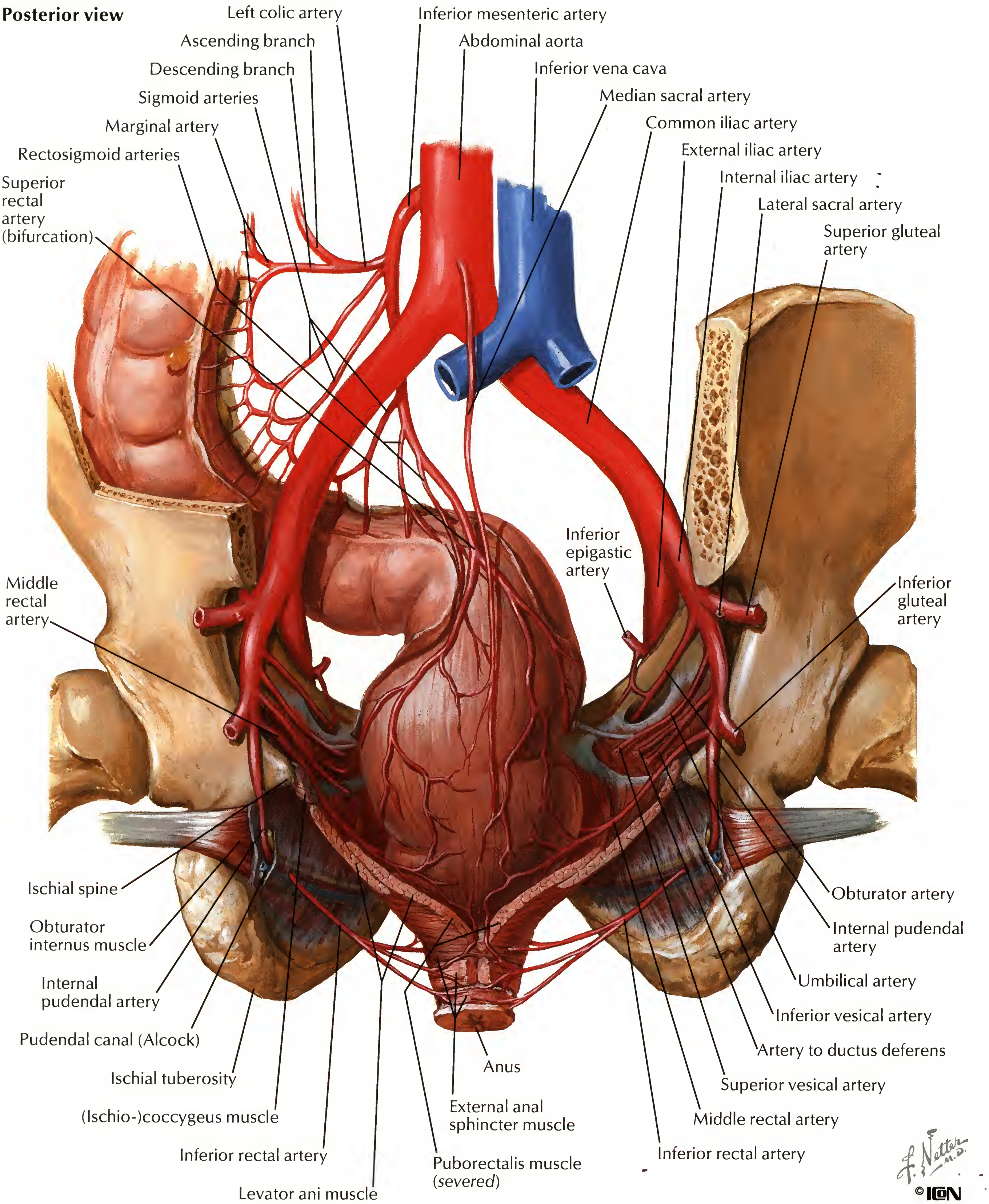
Absence of middle colic artery replaced by large branch from left colic artery



Absence of right colic artery



Arc of Riolan between middle colic and left colic arteries


Posterior view
Left colic artery
Ascending branch
Descending branch
Sigmoid arteries
Marginal artery
Rectosigmoid arteries
Superior rectal artery (bifurcation)
Inferior mesenteric artery
Abdominal aorta
Inferior vena cava
Median sacral artery
Common iliac artery
External iliac artery
Internal iliac artery
Lateral sacral artery
Superior gluteal artery
Middle rectal artery
Inferior epigastric artery
Inferior gluteal artery
Ischial spine
Obturator internus muscle
Internal pudendal artery
Pudendal canal (Alcock)
Ischial tuberosity
(Ischio-)coccygeus muscle
Inferior rectal artery
Levator ani muscle
Anus
External anal sphincter muscle
Puborectalis muscle (severed)
Obturator artery
Internal pudendal artery
Umbilical artery
Inferior vesical artery
Artery to ductus deferens
Superior vesical artery
Middle rectal artery
Inferior rectal artery
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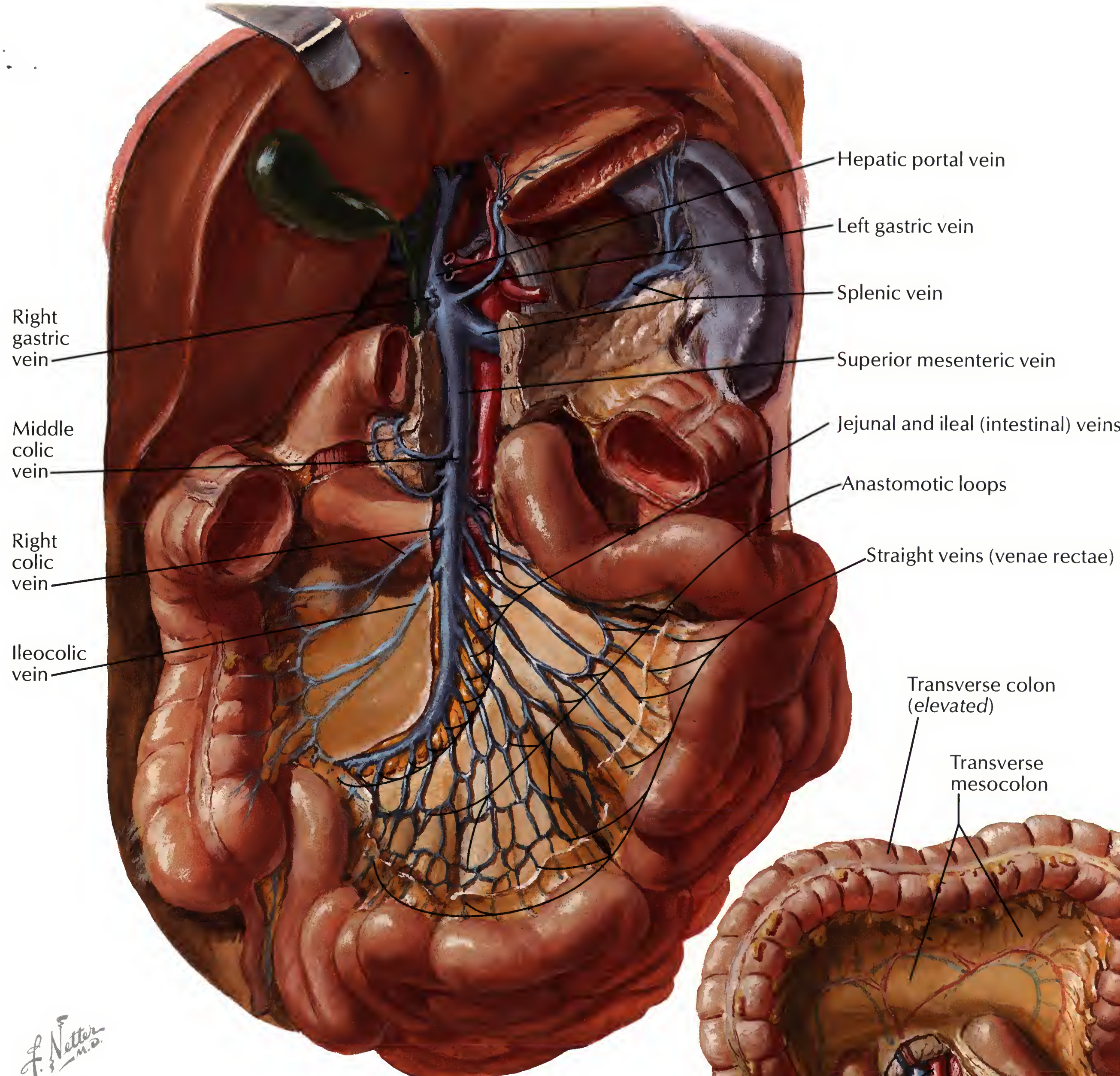
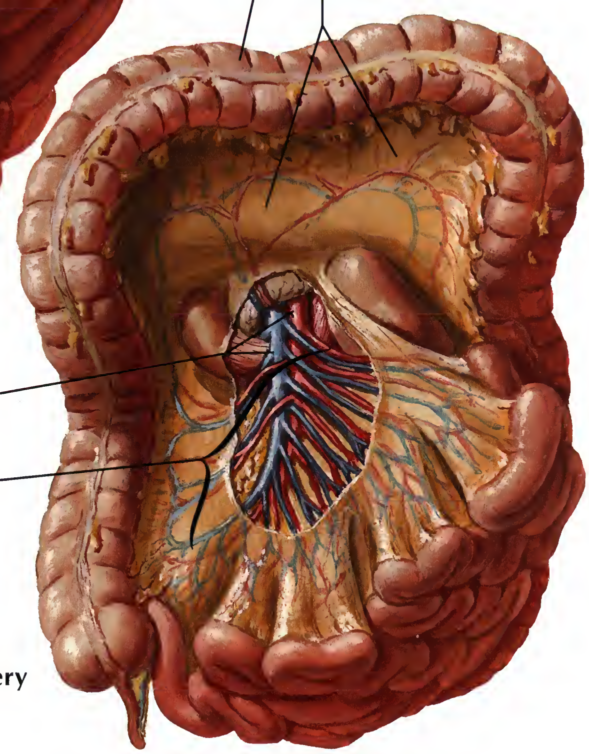
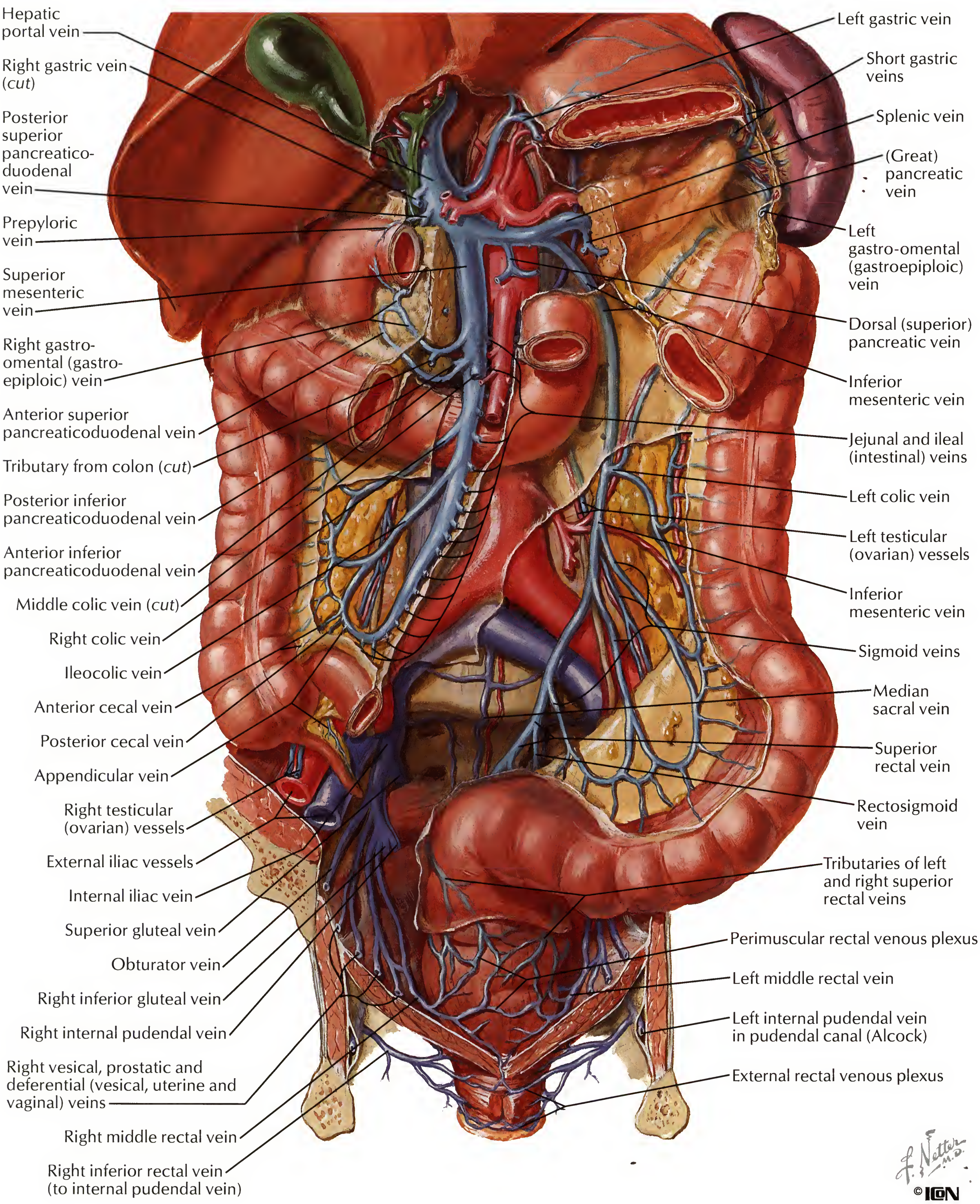
Veins of Small Intestine





Relations of superior mesenteric vein and artery in root of mesentery


Hepatic portal vein
Right gastric vein (cut)
Posterior superior pancreatico-duodenal vein
Prepyloric vein
Superior mesenteric vein
Right gastro-omental (gastro-epiploic) vein
Anterior superior pancreaticoduodenal vein
Tributary from colon (cut)
Posterior inferior pancreaticoduodenal vein
Anterior inferior pancreaticoduodenal vein
Middle colic vein (cut)
Right colic vein
Ileocolic vein
Anterior cecal vein
Posterior cecal vein
Appendicular vein
Right testicular (ovarian) vessels
External iliac vessels
Internal iliac vein
Superior gluteal vein
Obturator vein
Right inferior gluteal vein
Right internal pudendal vein
Right vesical, prostatic and deferential (vesical, uterine and vaginal) veins
Right middle rectal vein
Right inferior rectal vein (to internal pudendal vein)
Left gastric vein
Short gastric veins
Splenic vein
(Great) pancreatic vein
Left gastro-omental (gastroepiploic) vein
Dorsal (superior) pancreatic vein
Inferior mesenteric vein
Jejunal and ileal (intestinal) veins
Left colic vein
Left testicular (ovarian) vessels
Inferior mesenteric vein
Sigmoid veins
Median sacral vein
Superior rectal vein
Rectosigmoid vein
Tributaries of left and right superior rectal veins
Perimuscular rectal venous plexus
Left middle rectal vein
Left internal pudendal vein in pudendal canal (Alcock)
External rectal venous plexus
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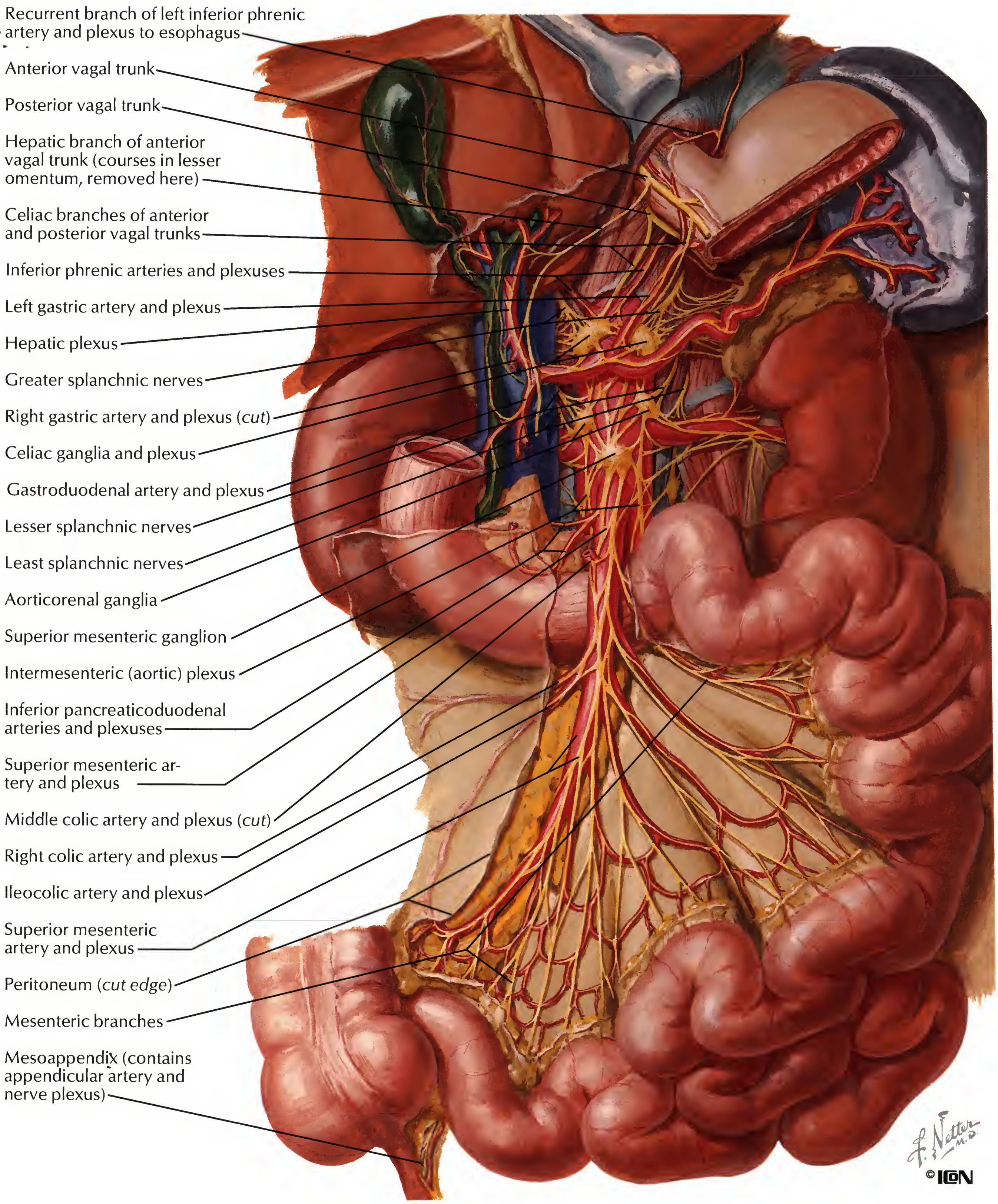
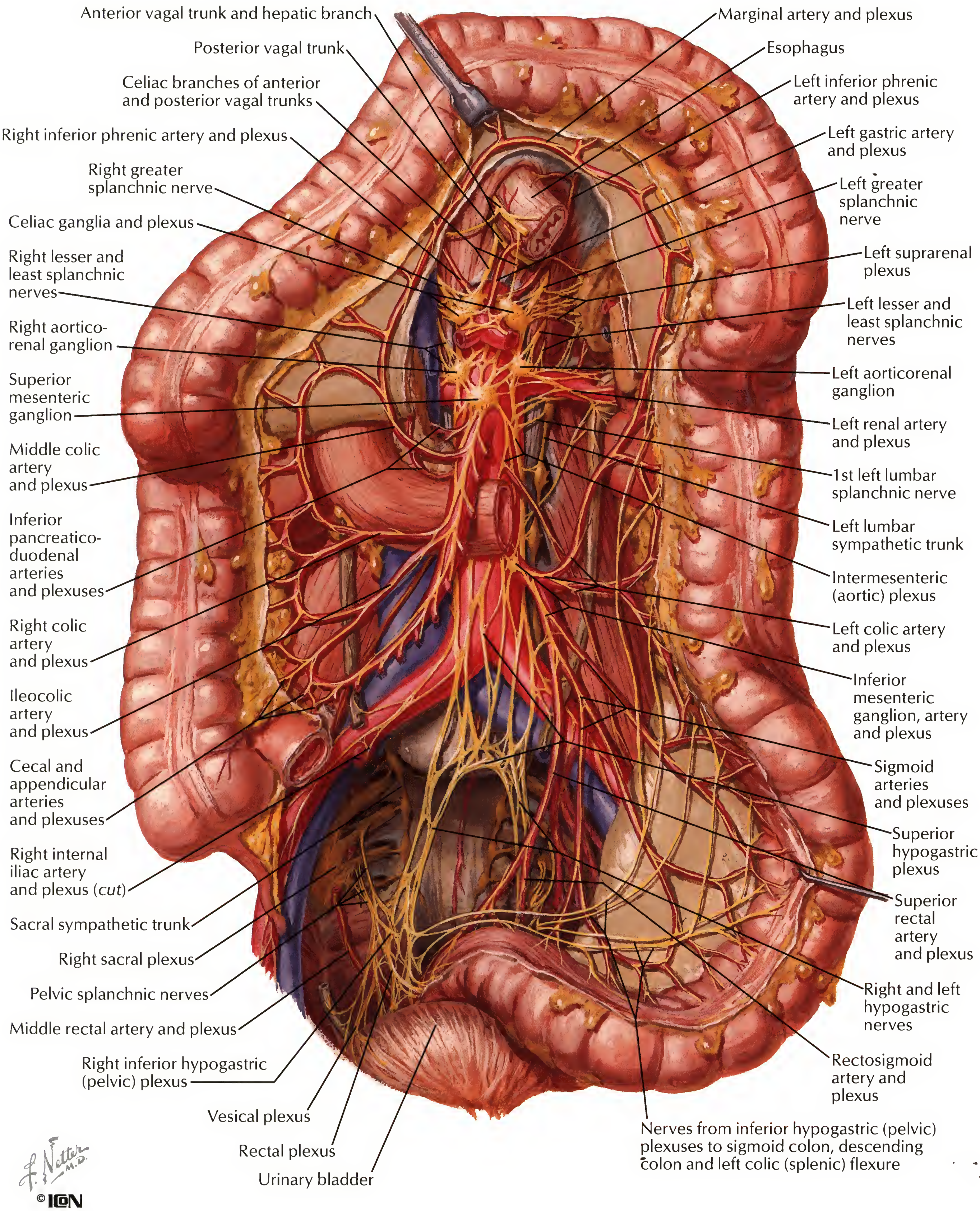
Nerves of Small Intestine




Anterior vagal trunk and hepatic branch
Posterior vagal trunk
Celiac branches of anterior and posterior vagal trunks
Right inferior phrenic artery and plexus
Right greater splanchnic nerve
Celiac ganglia and plexus
Right lesser and least splanchnic nerves
Right aortico-renal ganglion
Superior mesenteric ganglion
Middle colic artery and plexus
Inferior pancreatico-duodenal arteries and plexuses
Right colic artery and plexus
Ileocolic artery and plexus
Cecal and appendicular arteries and plexuses
Right internal iliac artery and plexus (cut)
Sacral sympathetic trunk
Right sacral plexus
Pelvic splanchnic nerves
Middle rectal artery and plexus
Right inferior hypogastric (pelvic) plexus
Vesical plexus
Rectal plexus
Urinary bladder
Marginal artery and plexus
Esophagus
Left inferior phrenic artery and plexus
Left gastric artery and plexus
Left greater splanchnic nerve
Left suprarenal plexus
Left lesser and least splanchnic nerves
Left aorticorenal ganglion
Left renal artery and plexus
1st left lumbar splanchnic nerve
Left lumbar sympathetic trunk
Intermesenteric (aortic) plexus
Left colic artery and plexus
Inferior mesenteric ganglion, artery and plexus
Sigmoid arteries and plexuses
Superior hypogastric plexus
Superior rectal artery and plexus
Right and left hypogastric nerves
Rectosigmoid artery and plexus
Nerves from inferior hypogastric (pelvic) plexuses to sigmoid colon, descending colon and left colic (splenic) flexure
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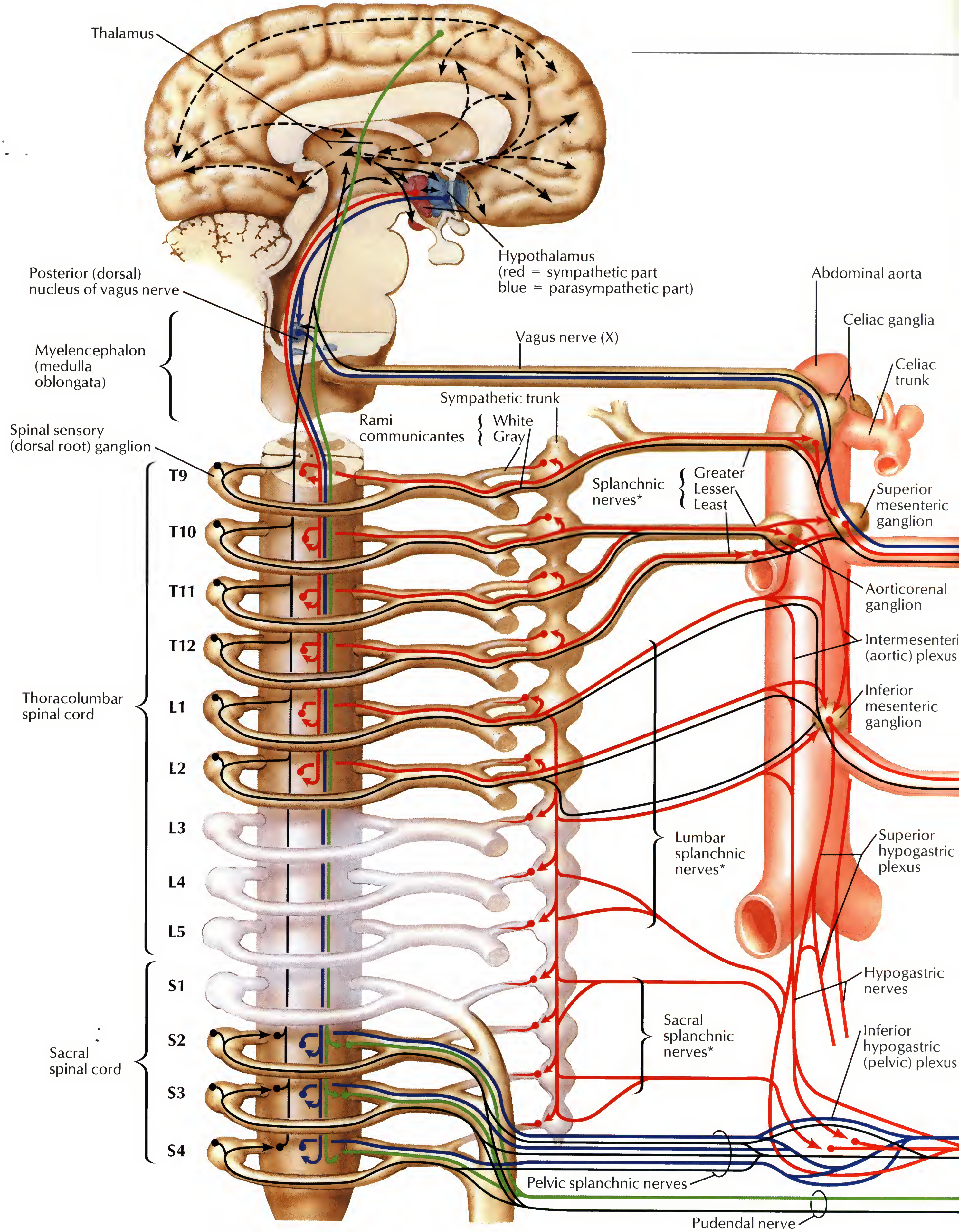
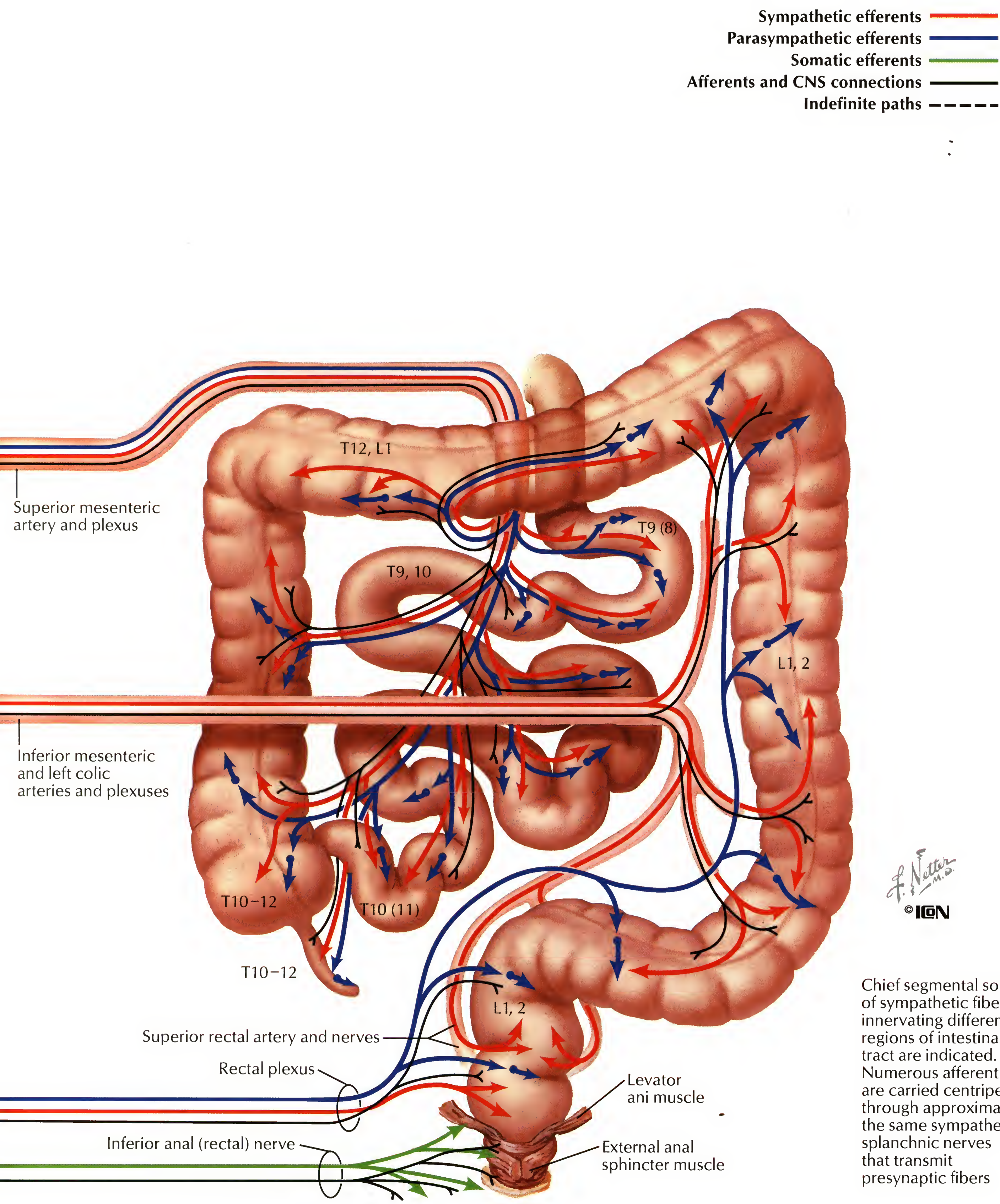


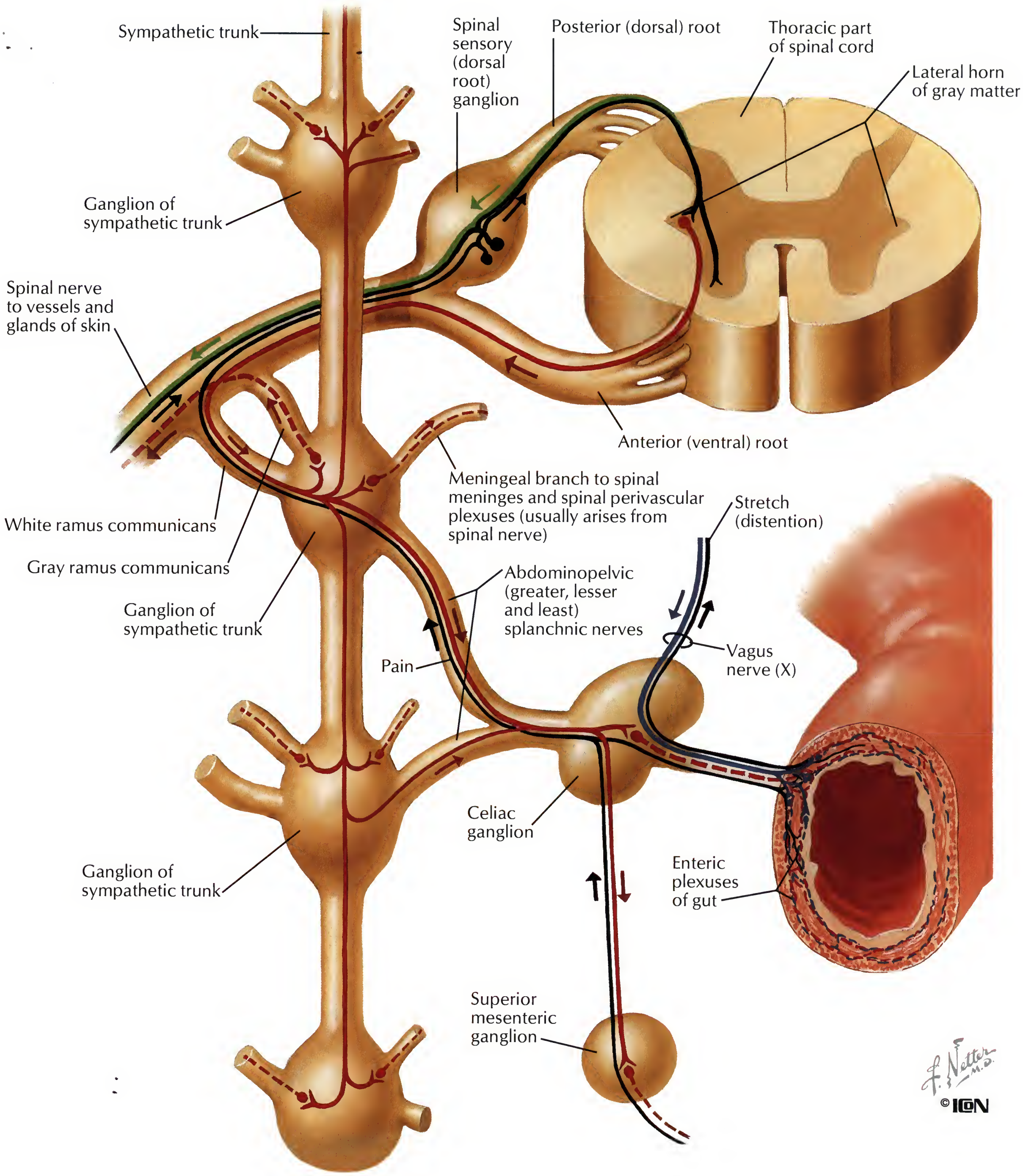
*Abdominopelvic splanchnic nerves

Innervation of Small and Large Intestines: Schema



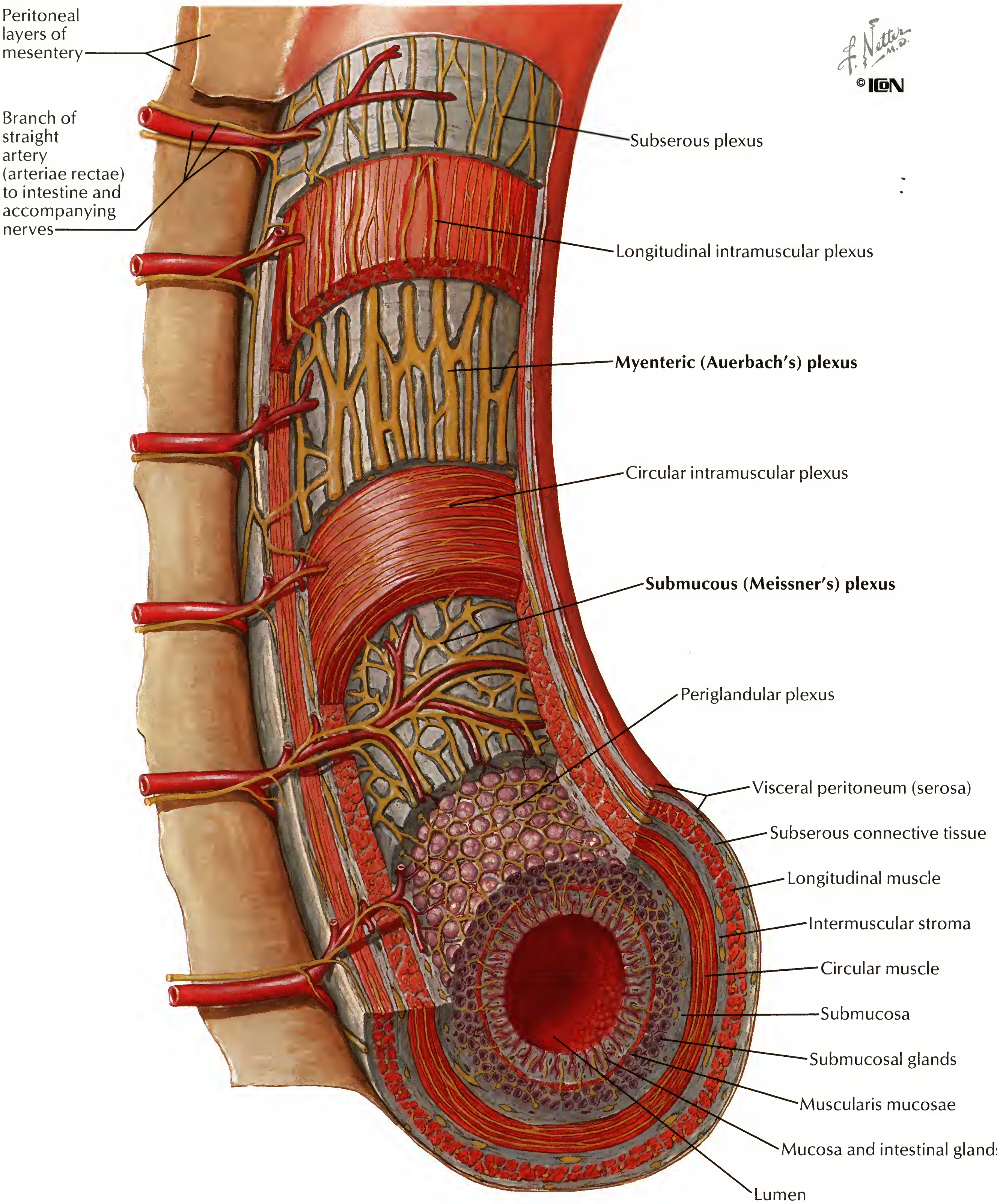
Chief segmental sources of sympathetic fibers innervating different regions of intestinal tract are indicated. Numerous afferent fibers are carried centripetally through approximately the same sympathetic splanchnic nerves that transmit presynaptic fibers

Autonomic Reflex Pathways: Schema



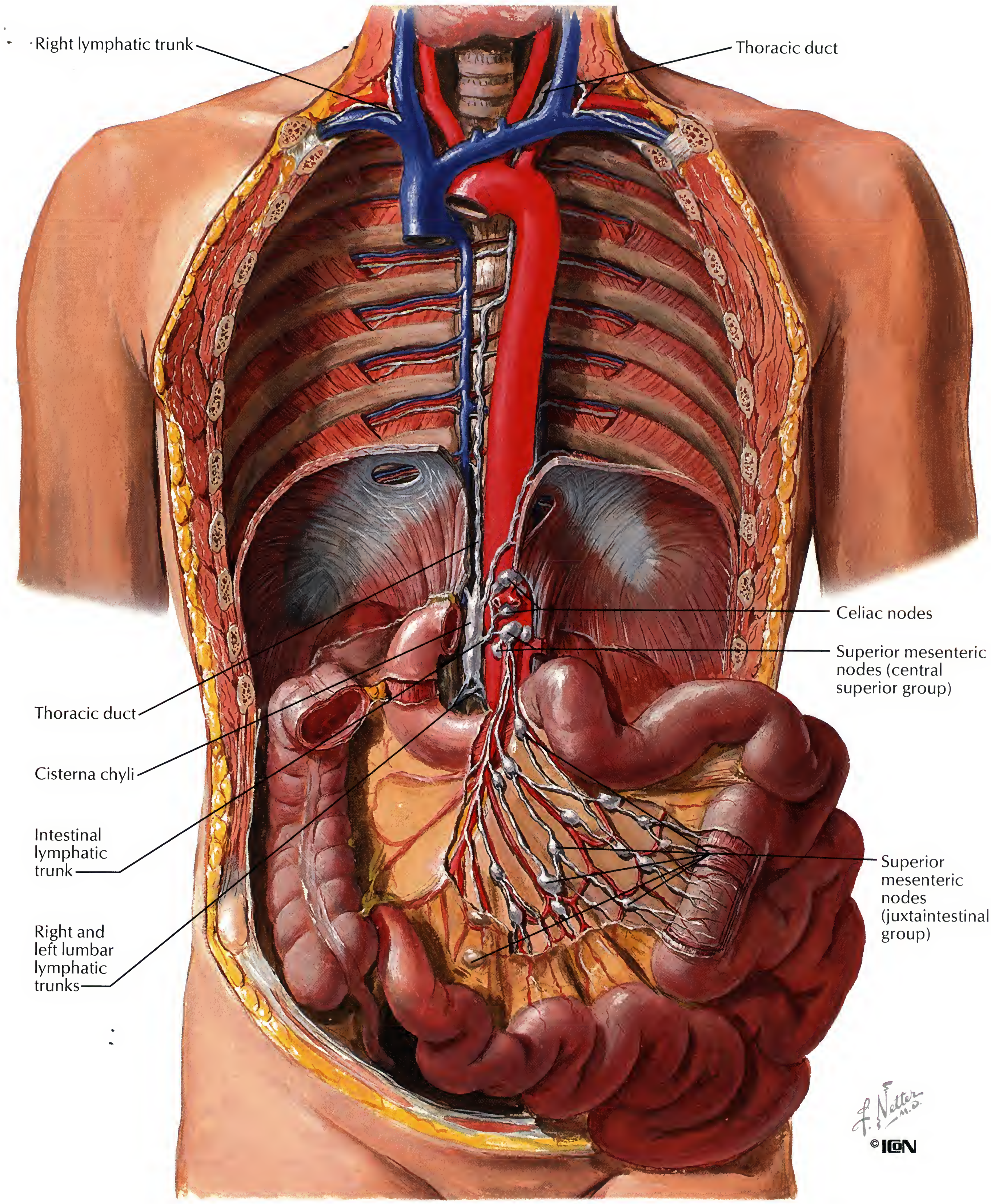
Sympathetic fibers	**Presynaptic** ———	**Postsynaptic** - - - - -	**Parasympathetic fibers**	**Presynaptic** ———	**Postsynaptic** - - - - -	
Afferent fibers ———	**Antidromic conduction** ———					

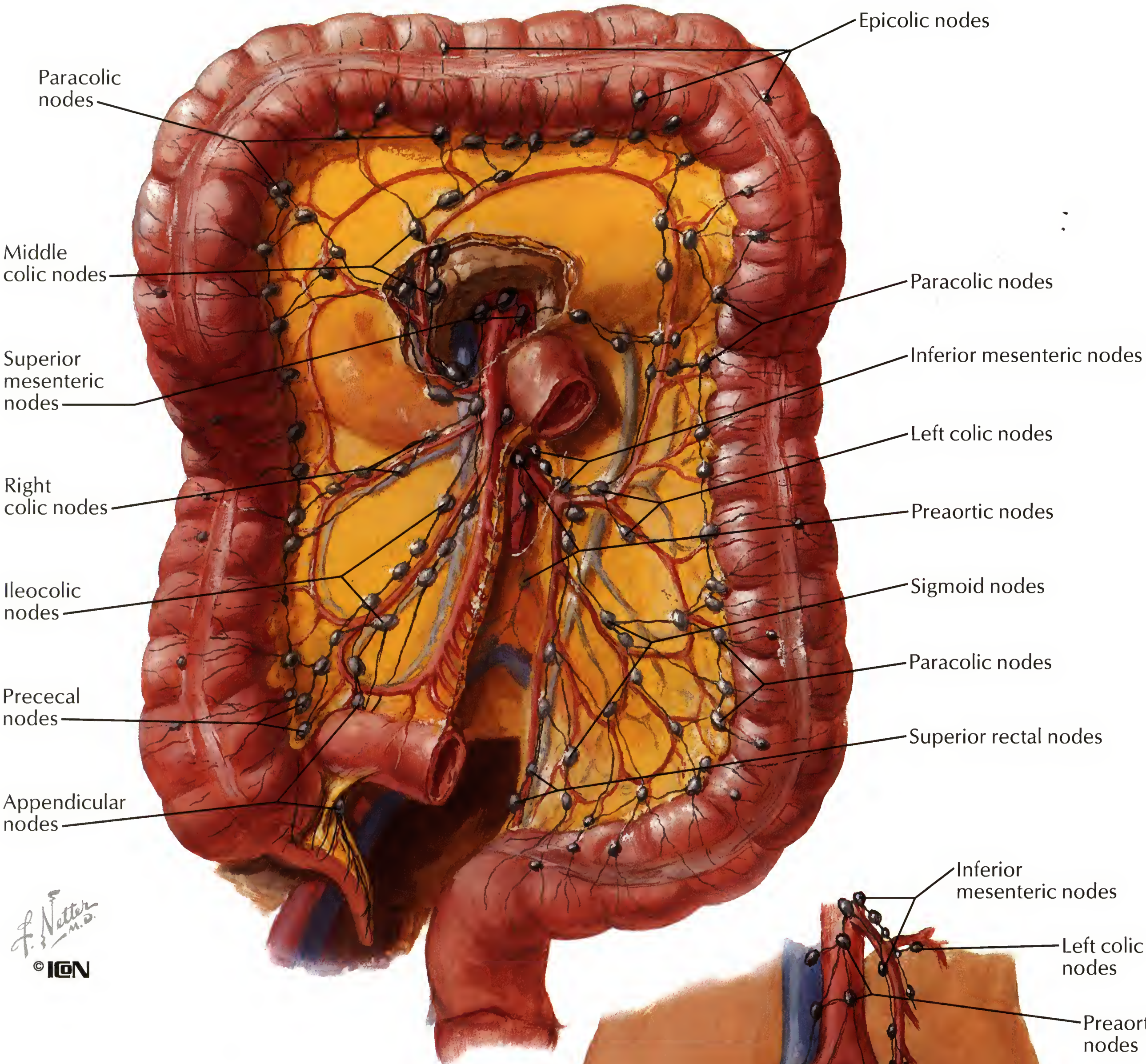
Intrinsic Autonomic Plexuses of Intestine: Schema



Note: Intestinal wall is shown much thicker than in actuality

Lymph Vessels and Nodes of Small Intestine




Epicolic nodes
Paracolic nodes
Middle colic nodes
Superior mesenteric nodes
Right colic nodes
Ileocolic nodes
Prececal nodes
Appendicular nodes
Paracolic nodes
Inferior mesenteric nodes
Left colic nodes
Preaortic nodes
Sigmoid nodes
Paracolic nodes
Superior rectal nodes
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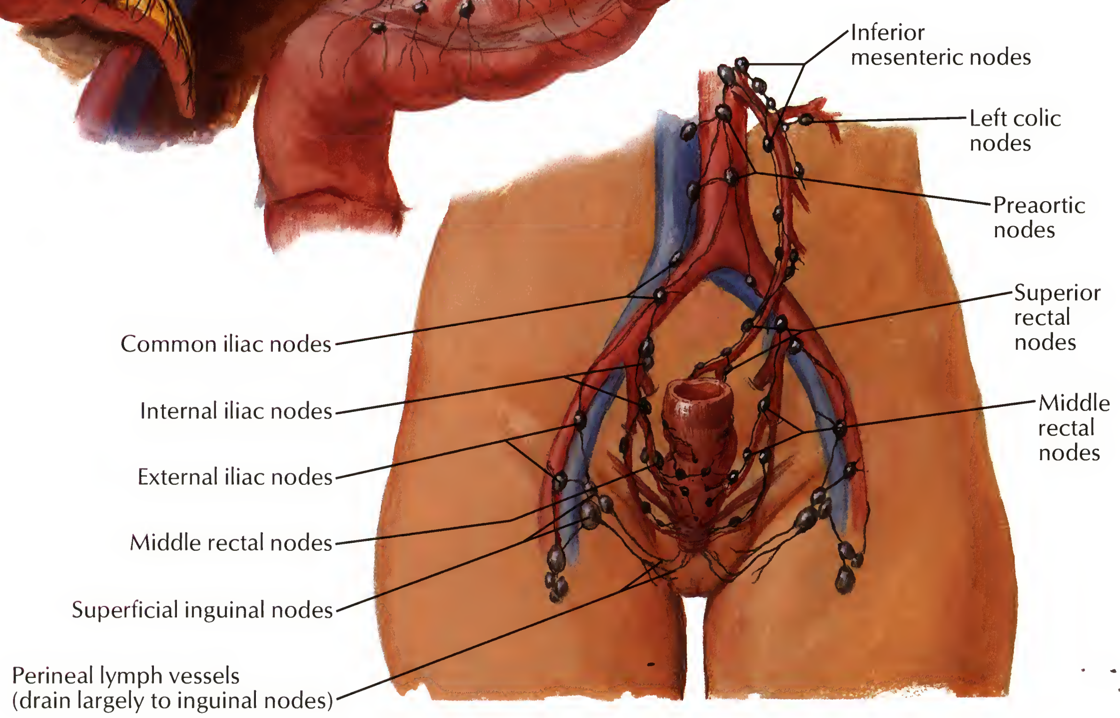
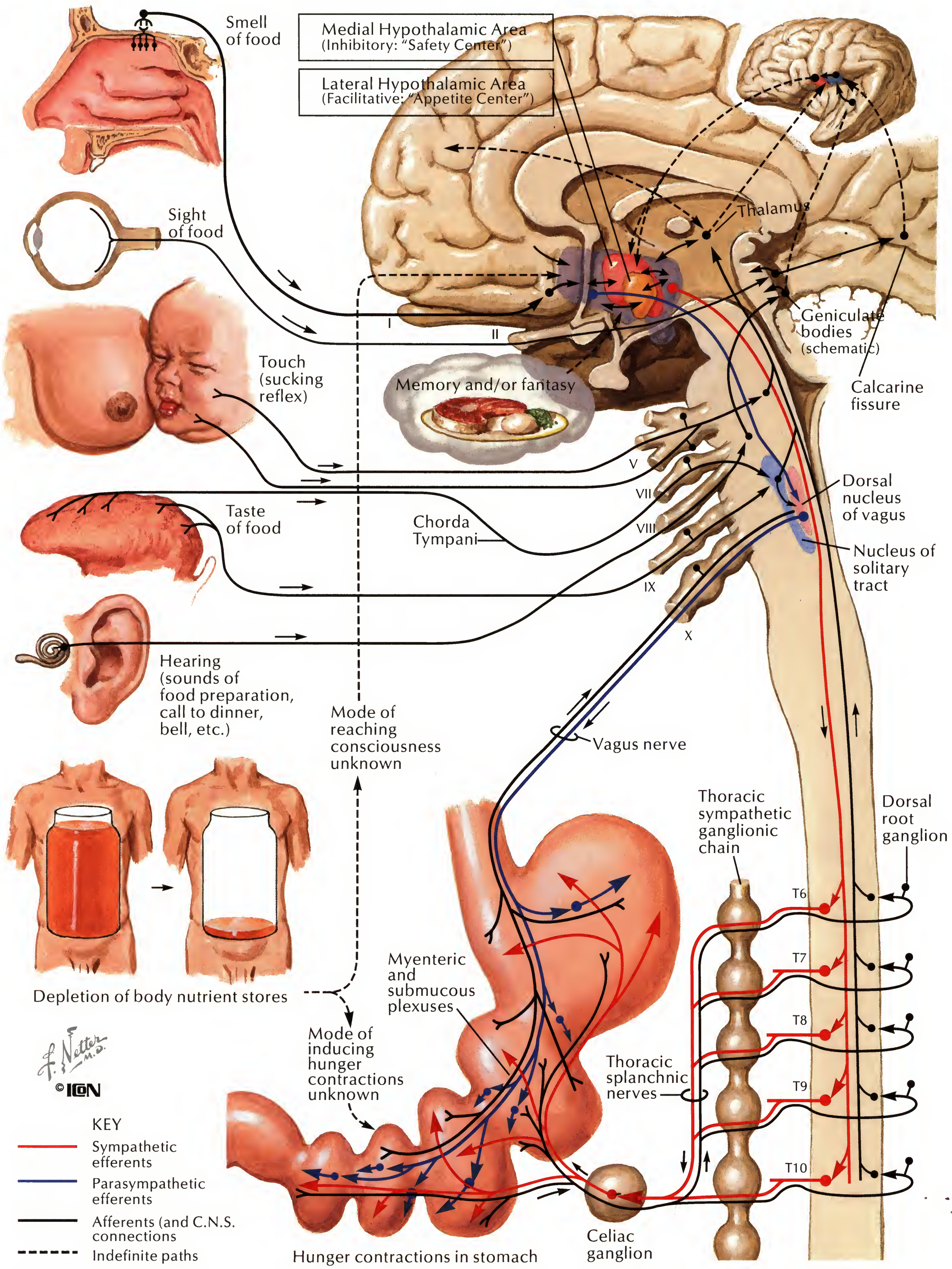

Inferior mesenteric nodes
Left colic nodes
Preaortic nodes
Superior rectal nodes
Middle rectal nodes
Common iliac nodes
Internal iliac nodes
External iliac nodes
Middle rectal nodes
Superficial inguinal nodes
Perineal lymph vessels (drain largely to inguinal nodes)

Hunger and Appetite

The digestive processes are initiated by the ingestion of food in response to need (hunger) or desire (appetite). Hunger has been defined as "the complex of sensations evoked by depletion of body nutrient stores" (Grossman). Of these sensations, the most common is a discomfort localized to the epigastrium and perceived as emptiness, gnawing, tension, or pangs. The epigastric sensation was at one time considered (Carlson) to be an indispensable element in hunger; but the fact that hunger is experienced by individuals whose stomach has been removed or denervated is evidence that contractions of the empty stomach (*hunger contractions*) cannot be an essential component of the hunger phenomenon. Hunger engenders a desire for food (appetite), which leads to appetitive behavior, manifested in the uncon-ditioned state, as in the newborn or anencephalic infant or decerebrate animal, by feeding reflexes, and in the conditioned or learned state by food-seeking and food-taking activities of varying complexity. Appetitive behavior is suppressed by the sensation of fullness or satiety brought on by adequate repletion with foodstuff.

The nervous regulation of all activities involved in obtaining and ingesting food has been thought, since Pavlov's investigations (1911), to be "centered" in *cell groups in the cerebral hemispheres* and at lower levels in the brain. According to one theory (Carlson), contractions of the empty or nearly empty stomach, activated by inherent automatism, give rise to impulses that pass up the *vagi* to the *nucleus solitarius*, thence to the *hypothalamus* and, finally, to the cerebral cortex. Some of the hunger reflexes are considered to be mediated in the medulla. The presence of two centers in the diencephalon—one in the lateral hypothalamic area concerned with the facilitation of feeding reflexes, the other a *medial hypothalamic* inhibitory *area*—has been established (Brobeck). From these "appetite" and "satiety" centers, fibers have been assumed to descend and act upon the neurons of the pons, medulla, and spinal cord, which govern the muscles involved in appetitive behavior as well as the motility and secretion of the digestive organs. Such theory assumes that, when food is eaten, certain changes occur that suppress the activity of the *lateral hypothalamus*, thus decreasing appetite while stimulating the medial portion and thus promoting satiety. The searching for, the examin-ation of, and the ingestion or rejection of food involve other nervous reflex mechanisms, of which those provoked by *visual, olfactory*, and *auditory stimuli* must be mediated via cortical connections to the hypothalamus. *Tactile, gustatory*, and *enteroceptive stimuli* could act through infracortical pathways.

Since food-taking behavior is not abolished by denervation of the gastrointestinal tract, it is evident that "the composition of the blood is a stimulus for the food center" (Carlson). Efforts to identify specific metabolic or chemical changes that govern the intervals of food taken and the amount of food eaten have resulted in hypotheses such as the glucostatic-lipostatic theory (J. Mayer, 1955). According to this theory, the short-term or meal-to-meal regulation of food intake is concerned with the acute energy requirements and depends upon the operation of glucoreceptors sensitive to the rate of glucose utilization, as reflected in the arteriovenous glucose difference. It is further hypothesized that the long-term regulation of food intake, directed at stabilizing body weight, is accomplished by a lipostatic mechanism, which controls the daily mobilization of a quantity of fat proportional to the total fat content of the body. It is presumed that these glucostatic and lipostatic mechanisms influence hunger and appetite via the hypothalamus. The ultimate validity of such theories will depend on the results of investigations stimulated by them. Presently, not enough evidence is available to decide precisely what blood or tissue changes, or other factors, are responsible for the seeking and taking of food.


Smell of food
Medial Hypothalamic Area (Inhibitory: "Safety Center")
Lateral Hypothalamic Area (Facilitative: "Appetite Center")
Sight of food
Thalamus
I
II
Geniculate bodies (schematic)
Touch (sucking reflex)
Memory and/or fantasy
Calcarine fissure
V
VII
Dorsal nucleus of vagus
Taste of food
Chorda Tympani
VIII
IX
Nucleus of solitary tract
X
Hearing (sounds of food preparation, call to dinner, bell, etc.)
Mode of reaching consciousness unknown
Vagus nerve
Thoracic sympathetic ganglionic chain
Dorsal root ganglion
T6
T7
T8
T9
T10
Depletion of body nutrient stores
Myenteric and submucous plexuses
Mode of inducing hunger contractions unknown
Thoracic splanchnic nerves
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KEY
Sympathetic efferents
Parasympathetic efferents
Afferents (and C.N.S. connections)
Indefinite paths
Celiac ganglion
Hunger contractions in stomach

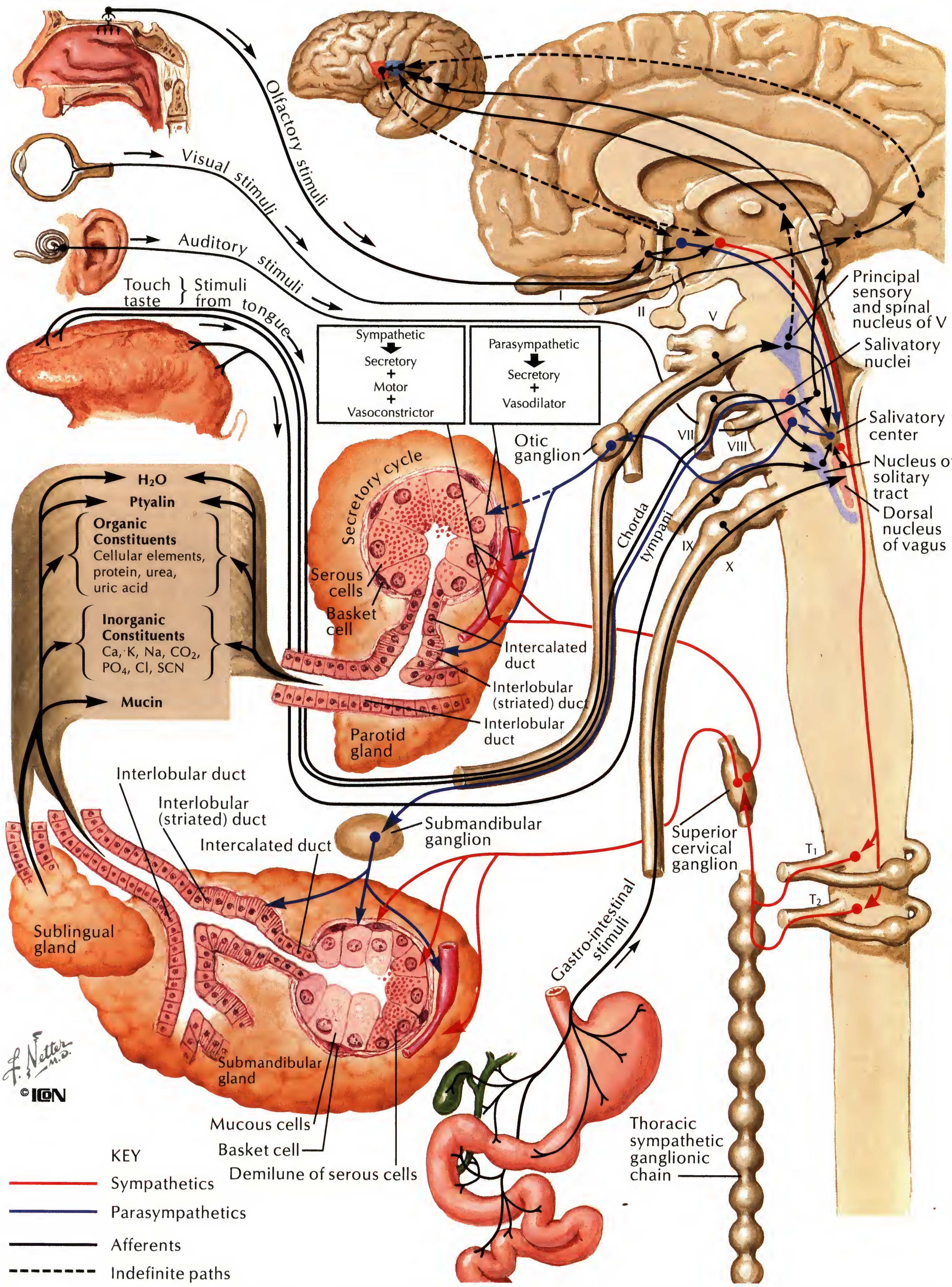
Salivary Secretion

Stimulation of areas in the *premotor region of the cortex cerebri* (in the vicinity of the masticatory center) and in the *hypothalamus* evokes salivation. No information is available as to nervous connections between these two areas or between the hypothalamus and the superior and inferior *salivary nuclei* in the medulla.

During the resting or recovery phase, when no secretory stimuli are acting, granules of mucinogen, the precursor of mucin, are formed in the mucous cells, and granules of zymogen, the precursor of ptyalin, in the serous or demilune cells. Extrusion of these substances, together with other components, into the lumen of the alveoli and into the ducts is activated entirely by impulses reaching the cells over the nervous pathways; no hormonal regulation of salivary secretion has been demonstrated. The *parasympathetic nerves* supply the mucin-secreting and the intralobular duct cells, while the *sympathetics* govern the serous cells and the myoepithelial or *"basket"* cells, which lie between the basal membrane and the secretory cells and are presumed to account for the contractile action that permits a gush of saliva. The quantity and composition of saliva are adapted to the nature of the agent that stimulates, chemically or mechanically, the nerve endings (V and IX) of the oral mucosa (unconditioned reflex). Thus, edible substances generally produce a viscid saliva, rich in mucin and enzyme. Inedible substances, e.g., sand, evoke a watery secretion. Acid material stimulates saliva with buffering (high protein content) and diluting properties. Milk, in contrast to other fluids, evokes a copious flow of saliva, rich in organic material—a fact that has been thought (Pavlov) to help the digestion of coagulum by the gastric juice. These unconditioned reflex responses do not depend on any learning process and have been elicited experimentally in decerebrated animals. The conditioned reflexes, on the other hand, are manifested by the flow of saliva in association with the thought or sight of food and with events the individual has learned to relate to food, such as the sound of a tuning fork in Pavlov's famous experiment with dogs.

The total amount of saliva secreted per day is estimated at 1000 to 1500 mL. The specific gravity varies from 1003 to 1008 and the pH from 6.2 to 7.6. Resting saliva is usually acid; freely flowing, usually alkaline. The viscosity varies with the type of stimulus and the rate of flow. The *parotid gland* forms a watery fluid containing protein, salts, and ptyalin, but no mucus. The *sublingual gland* is predominantly mucous, while the *submandibular* is intermediate, though predominantly serous in man. Saliva is hypotonic, and its osmotic pressure increases as flow rate increases. The only salivary enzyme, *ptyalin*, is produced by the parotid and submandibular glands and converts cooked starch into dextrins and maltose at a pH range of 4.5 to 9 (optimum 6.5). Ptyalin is inactivated at pH below 4.5 and destroyed by heating to 65°C. Other *organic constituents* include cellular elements from the buccal mucosa and the glands, urea, uric acid, and traces of urease. The *inorganic constituents* consist of the anions Cl-, PO4-, and HCO3- and the cations Ca, Na, and K. The ratio of the last two in the saliva mirrors their presence in the blood serum. Also present in the saliva is a small amount of thiocyanate, which is assumed to act as a coenzyme, since it can activate ptyalin in the absence of NaCl. The saliva of smokers is relatively rich in KCNS.

Saliva has a cleansing action that plays a significant role in oral hygiene, but the salivary glands have a still more important function inasmuch as they present an essential regulative factor for the water balance. The glands stop secreting saliva whenever the body fluid content falls to a low level, and this leads to a dryness of the oral mucosa and, therewith, arouses the sensation of thirst.



Olfactory stimuli
Visual stimuli
Auditory stimuli
Touch } Stimuli
taste } from tongue
Sympathetic
Secretory
+
Motor
+
Vasoconstrictor
Parasympathetic
Secretory
+
Vasodilator
I
II
V
Principal sensory and spinal nucleus of V
Salivatory nuclei
Salivatory center
Nucleus of solitary tract
Dorsal nucleus of vagus
Otic ganglion
VII
VIII
IX
X
Chorda tympani
H_2O
Ptyalin
Organic Constituents
Cellular elements, protein, urea, uric acid
Inorganic Constituents
Ca, K, Na, CO_2, PO_4, Cl, SCN
Mucin
Secretory cycle
Serous cells
Basket cell
Intercalated duct
Interlobular (striated) duct
Interlobular duct
Parotid gland
Interlobular duct
Interlobular (striated) duct
Intercalated duct
Submandibular ganglion
Superior cervical ganglion
T_1
T_2
Sublingual gland
Gastro-intestinal stimuli
Submandibular gland
Mucous cells
Basket cell
Demilune of serous cells
Thoracic sympathetic ganglionic chain
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KEY
Sympathetics
Parasympathetics
Afferents
Indefinite paths

Motility of Stomach, Empty Stomach, Filling of Stomach, Emptying of Stomach, and Duodenal Motor Activity

The following text was prepared in 1959 by William H. Bachrach, M.D., Ph.D, for the first edition of Volume 3, Part I of The Netter Collection of Medical Illustrations. *Since then, much has been learned about gastrointestinal motility and motor activity that was not available to Dr. Bachrach. We present this text both for its historical interest and to demonstrate to the reader the remarkable advances that have taken place over the past four decades in the science of gastrointestinal physiology.*

The internal pressure of the empty stomach, as recorded by appropriate techniques (e.g., balloon introduced into stomach, connected with manometer recording on a kymograph), changes periodically and with sufficient consistency to suggest distinct types of contractions. The interdigestive or "hunger" periods frequently begin with mild, rhythmic pressure waves occurring at a rate of three per minute, a pattern designated as *tonus rhythm* (Carlson), indicating that it represents regular changes in the tonus or state of gastromuscular tension. After a variable period of time, higher pressure elevations are recorded that appear as spikes of about 30 seconds' duration occurring at progressively closer intervals. These waves, termed Type I contractions, are assumed to represent *peristaltic contractions* originating at or proximal to the incisure and passing down to the pylorus. As the activity of the empty stomach becomes more vigorous, the contraction waves succeed each other at such a rate that new pressure waves are superimposed upon previous ones (Type II contractions). In occasional individuals, especially after periods of prolonged fasting, the gastric motility increases and exhibits a Type III contraction (also termed *"gastric tetanus"*), which is characterized by rapid passage of peristaltic waves along a stomach in a state of sustained tonus.

The cause of this motor activity of the empty stomach is not known, but, since it is present (though less vigorous) in the denervated stomach, it is assumed that the intrinsic nerves could serve as an autonomous pacemaker. The possibility of a humoral factor must be considered, because an autotransplanted fundic pouch contracts almost synchronously with the main stomach in experimental animals.

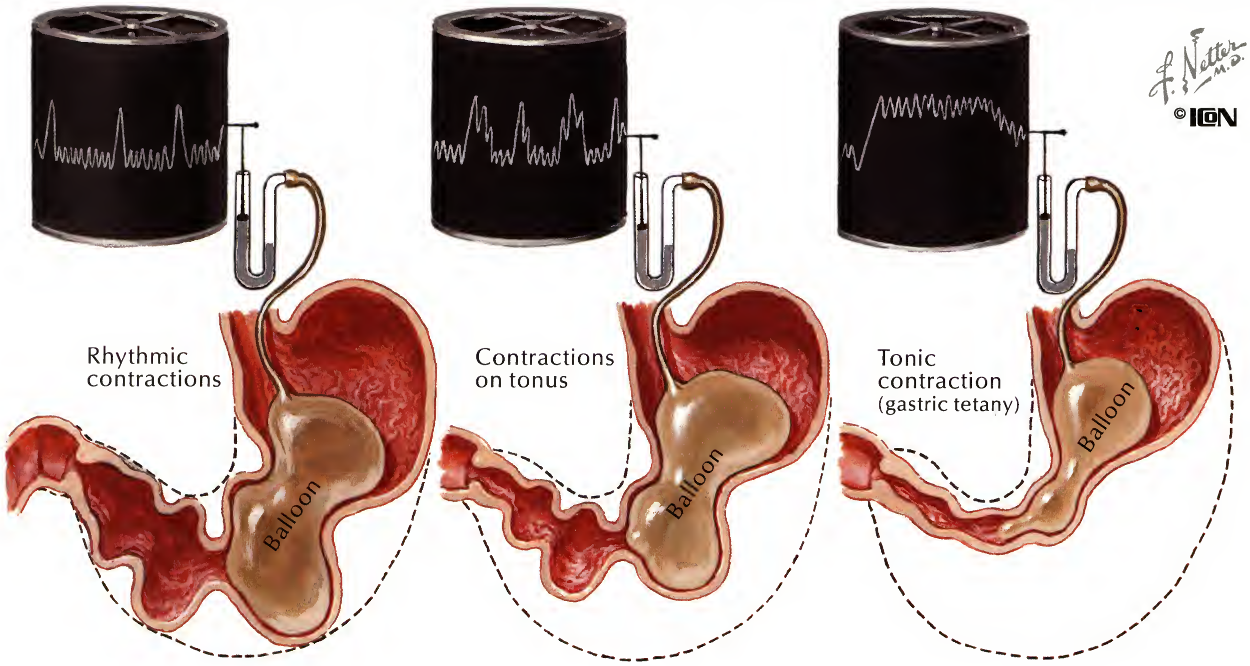
The "hunger" contractions of the empty stomach terminate when food is ingested. The cardiac and fundic regions relax in advance of the first swallowed bolus, and more so with the successive increments of food entering the stomach. This relaxation of the gastric musculature, manifesting its ability to elongate without change in tension, enables the stomach to enlarge to a volume adequate for a full meal, i.e., to serve as a reservoir. Together with the slackening of the abdominal muscles, which occurs as the stomach fills, this "receptive relaxation" also accounts in great measure for the *constancy of the intragastric pressure* while a meal is being eaten. Food entering the stomach passes down to the most dependent part. Successive portions of ingesta occupy the more central part of the mass, so that a sort of crude layering of the gastric content ensues. *Fluids* taken *when food is in the stomach* temporarily float on top, but soon gravitate down to the distal portion, whence they are promptly evacuated.

Peristalsis commences usually within a matter of minutes after food reaches the stomach, at first in the pyloric portion, which, owing to the greater thickness of its musculature, has the strongest triturating power. The contractions, as seen fluoroscopically in the presence of an opaque medium, originate as *shallow indentations in the region of the incisura angularis* and deepen as they move toward the pylorus. After 5 or 10 minutes, the contractions start at higher levels on the stomach and become progressively more vigorous. The pylorus, during this phase, opens only incompletely and intermittently as the waves advance toward it. Most of the material reaching the pyloric portion is forced back into the fundus, this process continuing until part of the content has been reduced to a fluid or semifluid consistency suitable for the small intestine. The evacuation is regulated, once the gastric content has the correct consistency, by the influence of the chyme in the upper intestine, where any adverse mechanical (too-rapid distention) or physicochemical (osmotic, pH) impact gives rise to intrinsic or extrinsic nervous reflexes, which modify the tone of the pyloric sphincter as well as the motor activity of the pyloric region. "The tonus of the pyloric sphincter in gastric emptying is chiefly determined by stimuli affecting the stomach muscle as a whole. Hence, its tonus changes are in the same direction and not opposed to the tone changes of the remainder of the pars pylorica. It serves as a constant resistance to the passage of chyme and blocks the exit of solid particles. By maintaining a narrow orifice it 'filters' the gastric contents. By contracting when the duodenum contracts, it limits regurgitation" (Thomas).

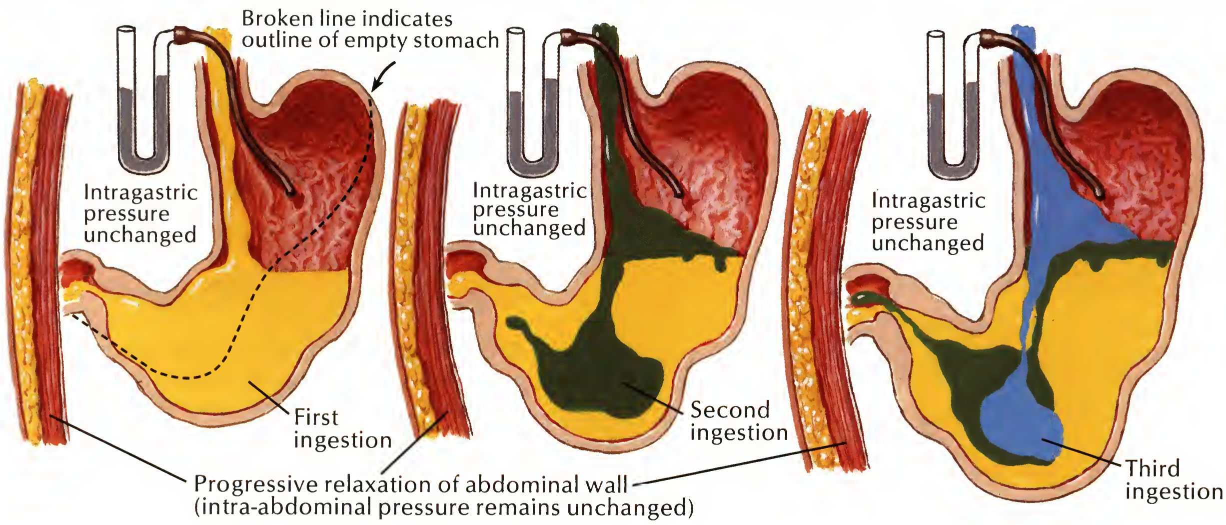
Ordinarily, gastric emptying proceeds smoothly while well-masticated food, free of gross irritants, is exposed to the digestive effect of the gastric secretion. Mechanical interference is minimized by the consistency to which the gastric chyme is reduced by the triturating effect of the gastric movements and the solubilizing effect of the secretory products.

"Receptive relaxation" of the first part of the duodenum permits the gastric content to be admitted without excessive distention. Physicochemical irritation by the gastric acidity is counteracted by the diluting and neutralizing actions of the secretion of the Brunner's glands and of the bile and pancreatic juice. The relaxation of the bulb persists during a series of gastric contractions, allowing the material to be pushed through it and into the second duodenal portion, where peristaltic waves develop. *Antral* and *duodenal contractions* seem to be fairly well synchronized (Wheelon and Thomas), apparently by intrinsic nervous reflexes.

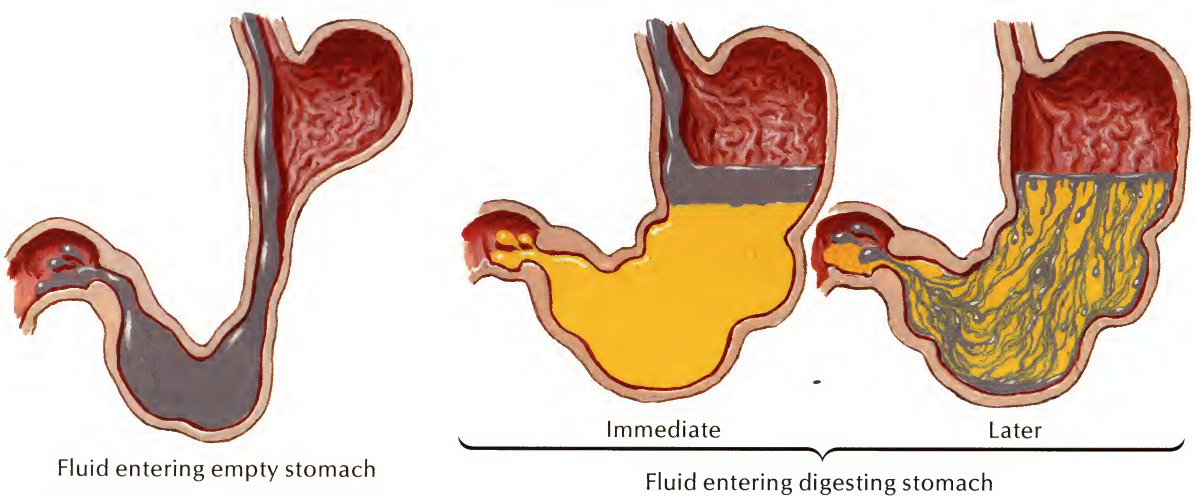
At the height of gastric propulsive activity, two peristaltic waves— occasionally three or four—may follow one another at intervals of from 5 to 15 seconds. This activity may continue without interruption or may be interspersed with periods of relative rest until the stomach is empty. Even before the gastric content has been completely evacuated, the motility characteristic of the "hunger period" (see above) may begin to develop.



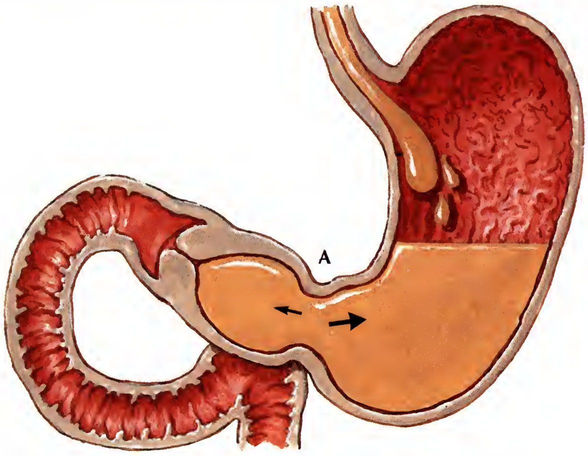
Movements of Empty Stomach



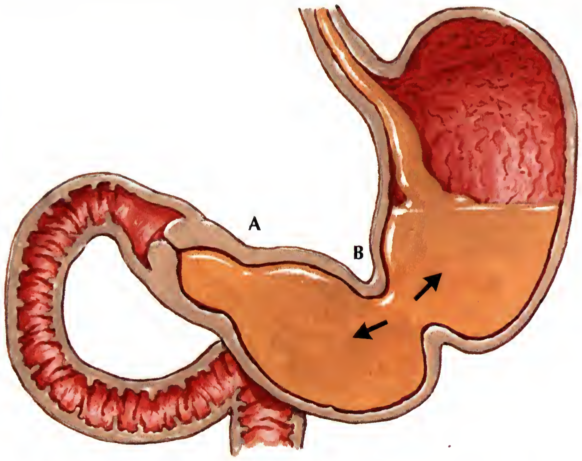
Gastric Filling



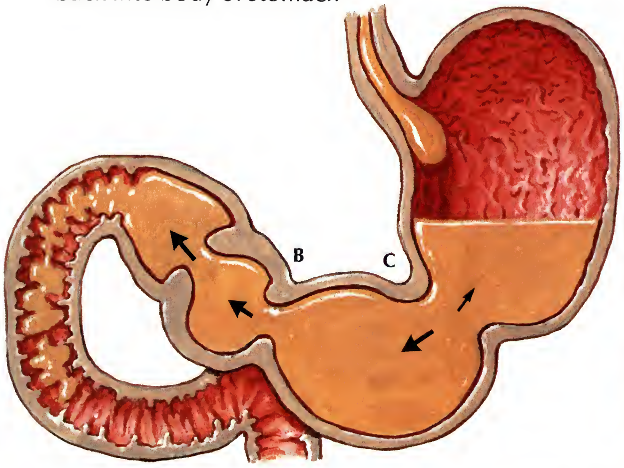
Motility of Stomach (continued)



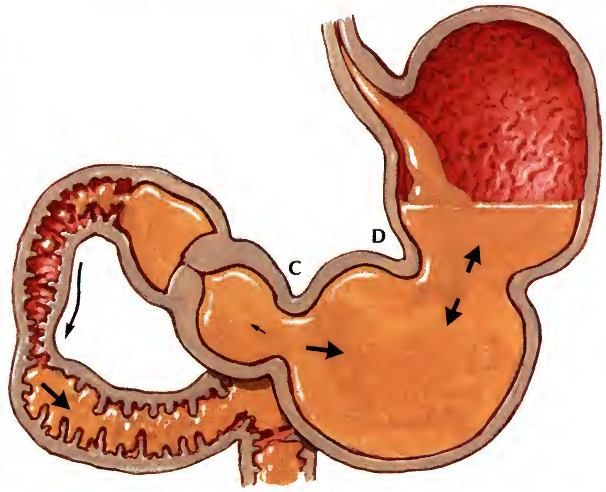
1. Stomach is filling. A mild peristaltic wave (A) has started in antrum and is passing toward pylorus. Gastric contents are churned and largely pushed back into body of stomach



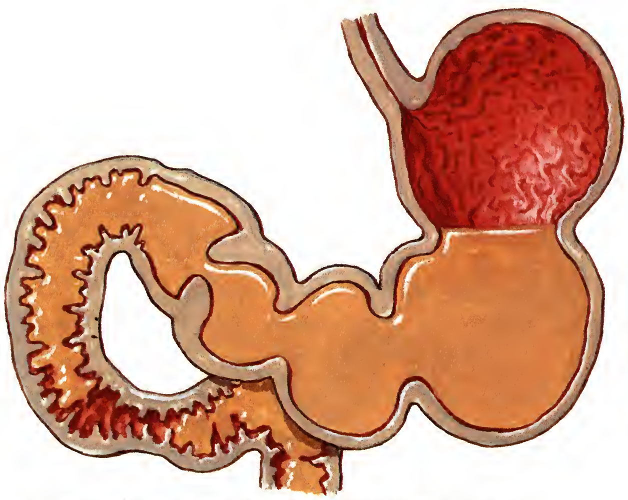
2. Wave (A) fading out as pylorus fails to open. A stronger wave (B) is originating at incisure and is again squeezing gastric contents in both directions



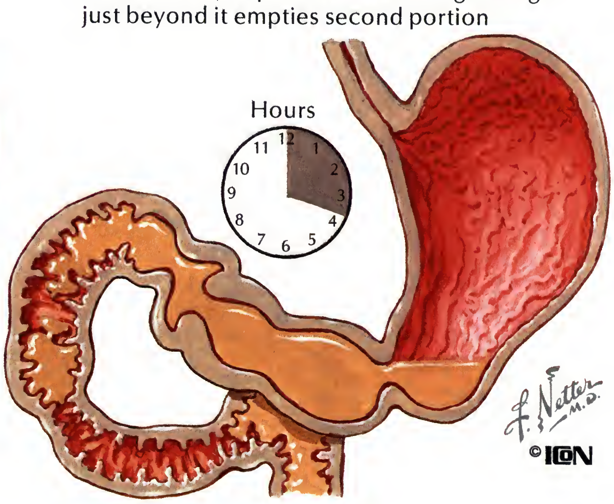
3. Pylorus opens as wave (B) approaches it. Duodenal bulb is filled and some contents pass into second portion of duodenum. Wave (C) starting just above incisure



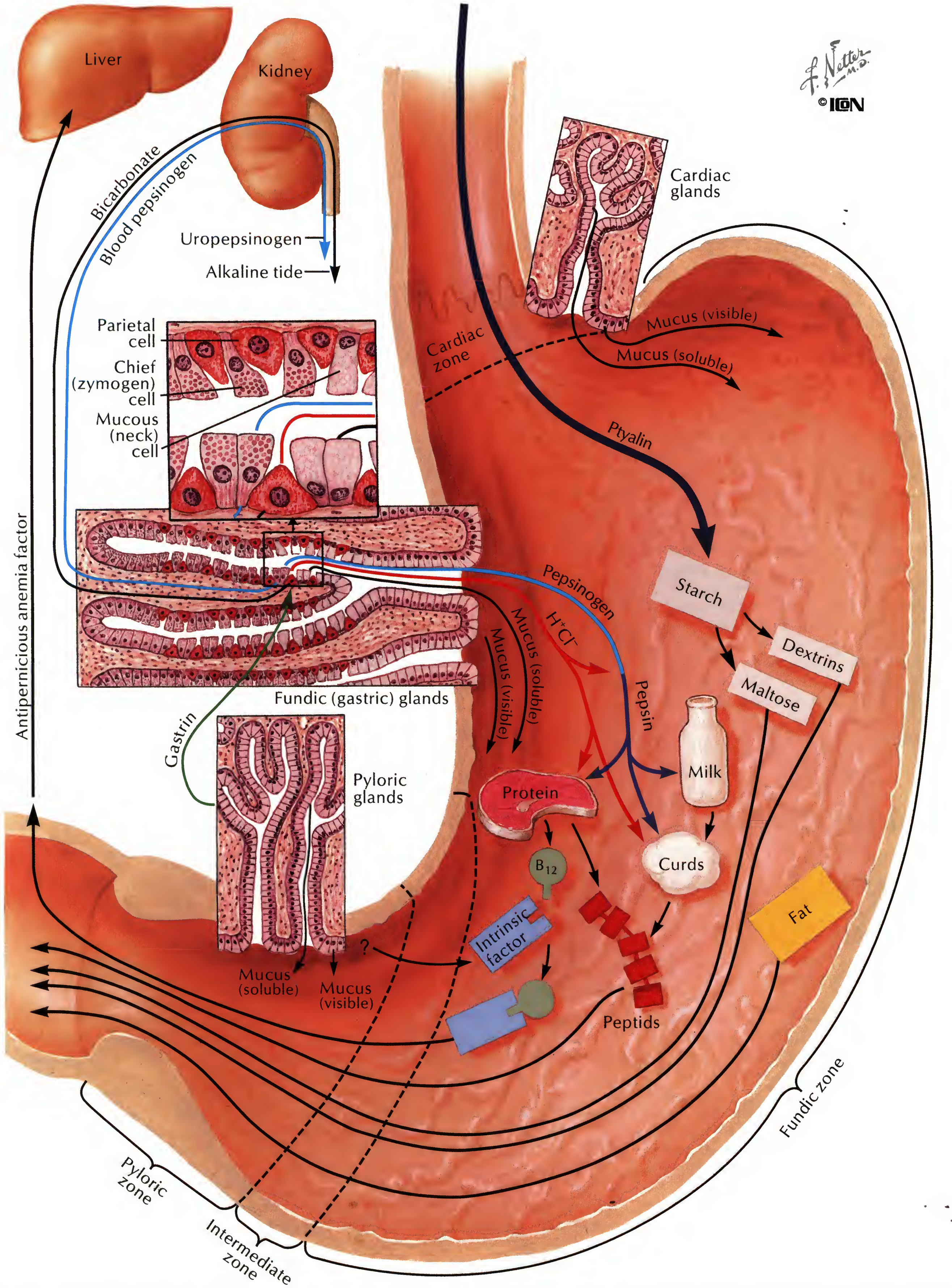
4. Pylorus again closed. Wave (C) fails to evacuate contents. Wave (D) starting higher on body of stomach. Duodenal bulb may contract or may remain filled, as peristaltic wave originating just beyond it empties second portion



5. Peristaltic waves are now originating higher on body of stomach. Gastric contents are evacuated intermittently. Contents of duodenal bulb area pushed passively into second portion as more gastric contents emerge



6. 3 to 4 hours later stomach almost empty. Small peristaltic wave emptying duodenal bulb with some reflux into stomach. Reverse and antegrade peristalsis present in duodenum



Liver
Kidney
Bicarbonate
Blood pepsinogen
Uropepsinogen
Alkaline tide
Parietal cell
Chief (zymogen) cell
Mucous (neck) cell
Antipernicious anemia factor
Fundic (gastric) glands
Gastrin
Pyloric glands
Mucus (soluble)
Mucus (visible)
?
Cardiac glands
Mucus (visible)
Mucus (soluble)
Cardiac zone
Ptyalin
Starch
Dextrins
Maltose
Pepsinogen
H⁺Cl⁻
Mucus (soluble)
Mucus (visible)
Pepsin
Milk
Protein
Curds
B12
Intrinsic factor
Fat
Peptids
Fundic zone
Pyloric zone
Intermediate zone
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Digestive Activity of Stomach (continued)

Almost all available evidence points to the parietal cell as the source of the *HCl of the gastric secretion.* The concentration of the acid, as it leaves the parietal cell, is in the neighborhood of 0.160 N; more common expressions for the same value are 160 mEq/L, and 160 clinical units or degrees of acidity. This theoretical maximal concentration of HCl is never actually attained, because the observed acidity at any given time depends upon the relative proportions of parietal and nonparietal secretions. In general, the more rapid the rate of secretion, the higher the acidity.

Aside from the normal physiologic mechanisms, a number of systemic and local factors affect the secretion of acid. The stimulating effect of the oral administration of sodium bicarbonate, popularly called "acid rebound," is probably the result of a combination of factors, including a direct stimulating action on the gastric mucosa, annulment of the antral acid-inhibitory influence, and acceleration of gastric emptying.

The *alkaline tide*, or decrease in urinary acidity that may occur after a meal, is generally attributed to an increased alkalinity of the blood resulting from the secretion of HCl. The occurrence of an alkaline tide is not predictable, being influenced by (1) the relative rate of formation of HCl and alkaline digestive secretions, mainly pancreatic with its high content of $NaHCO_3$; (2) the rate of absorption of HCl from the gut; (3) the neutralizing capacity of the food; (4) respiratory adjustments after the meal; and (5) the diuretic effect of the meal.

Pepsin, the principal enzyme of gastric juice, is preformed and stored in the chief cells as *pepsinogen*. At pH below 6, pepsinogen is converted to pepsin, a reaction that then proceeds autocatalytically; i.e., the free pepsin activates the continued transformation of pepsinogen to pepsin. Pepsin exerts its proteolytic activity by attacking peptid linkages containing the amino groups of the aromatic amino acids, with the liberation principally of intermediate protein moieties and very few polypeptids and amino acids. An accessory digestive function of pepsin is the *clotting of milk*, which serves to improve the utilization of this food by preventing its too-rapid passage through the alimentary tract and rendering it more susceptible to enzymatic hydrolysis. Anything that mobilizes vagal impulses to the stomach serves as a powerful stimulus for pepsin secretion; thus, a gastric juice rich in pepsin content is evoked by sham feeding, by hypoglycemia (which stimulates the vagal centers), or by direct electrical stimulation of the vagus nerves.

The pepsinogen of the gastric chief cells, besides being secreted externally into the lumen of the stomach, is to some extent secreted internally into the blood stream and appears in the urine as *uropepsinogen*, which provides the basis for attempts to use uropepsinogen determinations as an index of the peptic secretory activity of the stomach.

The mucoid component of gastric juice consists of at least two distinct mucoproteins. One of these substances, the so-called *"visible mucus,"* has a gelatinous consistency and, in the presence of HCl, forms a white coagulum; evidence indicates that it is secreted by the surface epithelium. The other, usually referred to as the *soluble*, or dissolved, *mucus*, appears to be a product of the neck chief cells and the mucoid cells of the pyloric and cardiac glands.

The secretion of soluble mucus is activated primarily by vagal impulses, while the secretion of visible mucus occurs principally in response to direct chemical and mechanical irritation of the surface epithelium. By virtue of its adherent properties and its resistance to penetration by pepsin, the mucous secretion protects the mucosa of the stomach against damage by various irritating agents, including its own acid-pepsin.

A normal constituent of the gastric juice, but characteristically deficient or absent in patients with pernicious anemia, is the *"intrinsic factor."* It interacts with cobalamine (vitamin B_{12}) to prepare it for absorption in the intestine.

The gastric juice, furthermore, contains the proteolytic enzyme, cathepsin, a weak lipase, urea, amino acids, histamine, and a number of inorganic ions (Na+, K+, Ca++, Mg++, Cl-, HCO3-, SO4=, and phosphates).

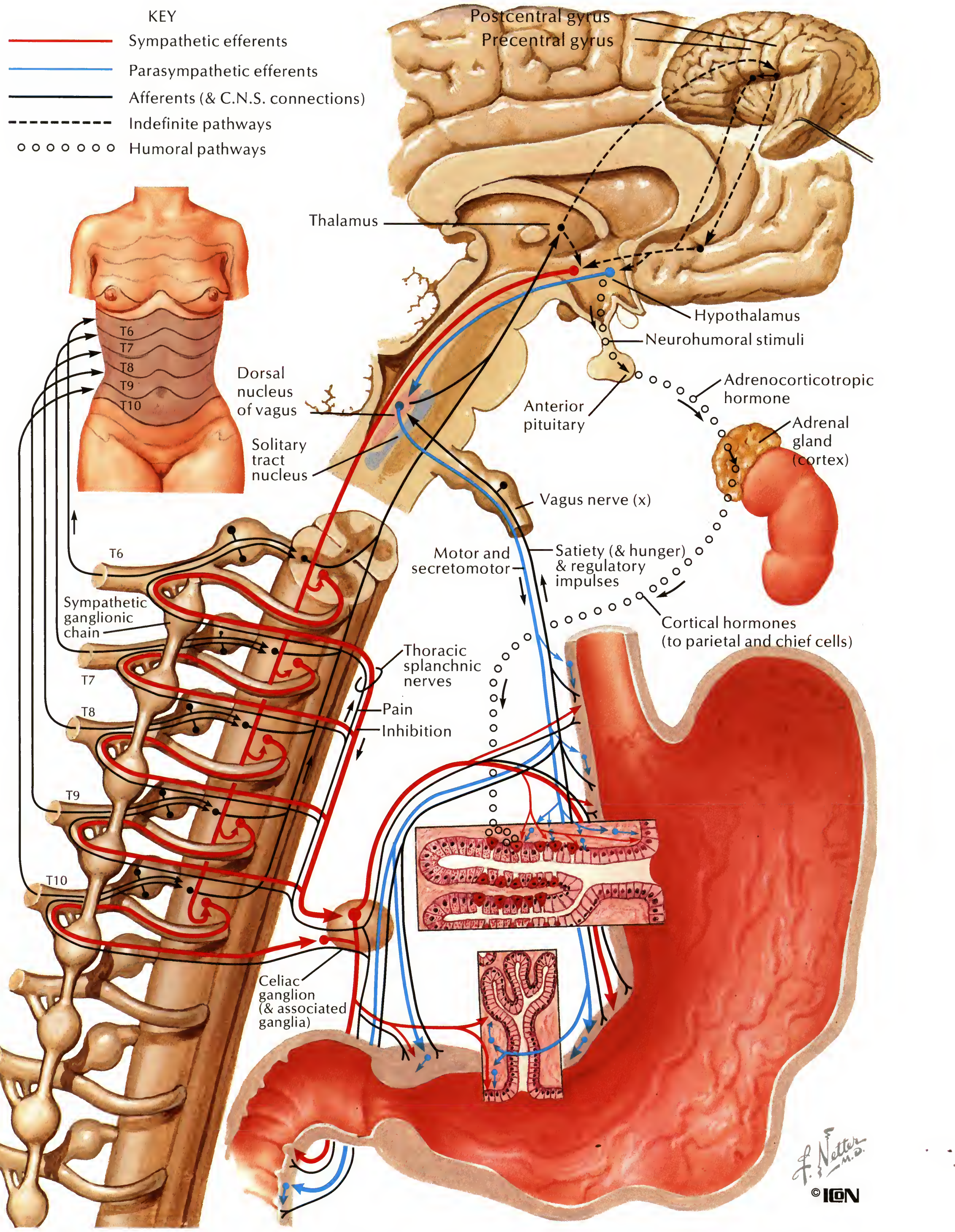
Neuroregulation of Gastric Activity

Such evidence as is available places the cortical area that influences gastric motility and secretion in the *posterior orbital gyrus* and the adjacent *anterior cingulate gyrus.* Connections are made, via the medial *thalamic nuclei*, with the *hypothalamus*, whence fibers descend in the dorsal longitudinal fasciculus, at least as far as the *dorsal nucleus of the vagus.* Impulses from the anterior hypothalamic region act, it is assumed, on the cranial *para-sympathetic nuclei in the brain stem*, while the posterior hypothalamus probably makes connections with the *neurons of the lateral horns* of gray matter in the thoracolumbar segments of the spinal cord.

The *vagi*, the principal innervation to the stomach, exert augmentative and inhibitory effects on both motility and secretion. Gastric tonus, motility, and secretory activity are permanently reduced when the vagi are sectioned, whereas section of the splanchnic nerve does not essentially alter the functions of the stomach.

The *afferent fibers*, which take their course with the vagi and sympathetic nerves, mediate the visceral sensations. Pain sensations are carried by afferent fibers accompanying the sympathetic nerves. In contrast to the somatic sensory nerves, the visceral afferents or their receptors are relatively insensitive to stimuli such as cutting or burning. The effective stimulus for visceral pain is thought to be medicated by tension transmitted to the nerve endings by strong muscular contraction, by distention or by inflammation. Normal peristaltic movements of the stomach do not ordinarily give rise to any sensation, but forceful contractions may be perceived as a feeling of gnawing and tension or as an actual pain in the abdomen, particularly in the presence of an inflammatory or ulcerative process. In addition to the discomfort that the individual locates in the involved viscus, pain may be felt that is subjectively interpreted as arising in the abdominal or thoracic wall. The *areas* to which this *"referred pain"* is ascribed depend upon the distribution of the afferent fibers and their course. Pain from the stomach is conveyed mainly in the afferents that run in the *sympathetic nerves of the fifth to the tenth thoracic segments*, but the pathways may also extend as low

as the twelfth. The impulses reach the spinal cord by way of the white communicating rami and the dorsal root ganglia. Pain originating in the stomach may be referred to any of the somatic structures receiving their sensory supply from the fifth to the twelfth thoracic segments. Many of the details of the visceral and "referred" pain remain to be clarified. Several theories and concepts still await unification and experimental confirmation.



Factors Influencing Gastric Activity

Motor and secretory activities of the stomach are modified, usually simultaneously and in the same direction, by a number of factors, chief among which are the following:

1. *TONUS OF THE STOMACH.* The *hypertonic*, or steer-horn, stomach tends to be hypermotile and to empty relatively rapidly, as contrasted with the *hypotonic*, or fishhook, type. Also, individuals with a hypertonic stomach tend toward secretion of more HCl and, as a corollary, to accelerated secretion and diminished intragastric stasis.

2. *CHARACTER OF THE FOOD.* A meal that is sufficiently high in fat to yield an intragastric fat content in excess of about 10 percent empties much more slowly and stimulates considerably less acid secretion than does a meal *predominantly of protein*. The inhibitory effect of fat on gastric secretion is not a local one, but a result of enterogastrone formation after fat has entered the upper intestine. A meal exclusively or *mainly of starch* tends to empty more rapidly, though stimulating less secretion, than does a protein meal. Thus, other factors being equal, a person may expect to be hungry sooner after a breakfast of fruit juice, cereal, toast, and tea than after one of bacon, eggs, and milk. The amounts of total secretion and of acid content are highest with the ingestion of proteins. However, the relationship of quantity and rate of secretion and its acid or pepsin concentration is subject to great individual variations, as well as to variations in a single individual under different conditions.

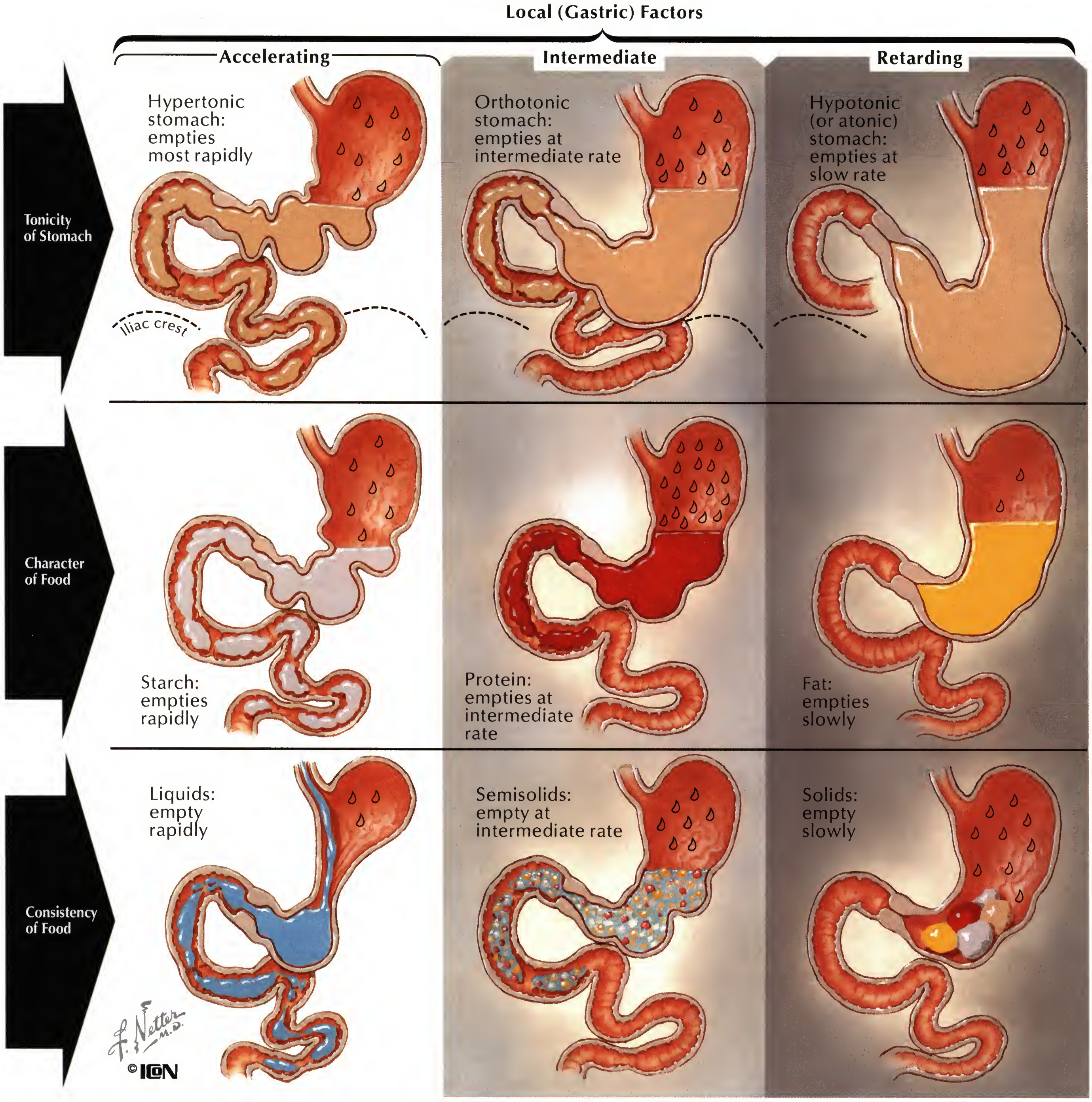
3. *CONSISTENCY OF THE FOOD.* *Liquids*, whether ingested separately or with solid food, leave the stomach more rapidly than do *semisolids* or *solids*. This does not apply to liquids such as milk, from which solid material is precipitated on contact with gastric juice. In the case of any foods requiring mastication, the consistency of the material reaching the stomach should normally be semisolid, thereby facilitating gastric secretion, digestion, and evacuation. Important exceptions to the general rule that liquids are weak stimulants of gastric secretion are (1) the broth of meat or fish, by virtue of their high secretagogue content, and (2) coffee, which derives its secretory potency from its content both of caffeine and of the secretagogues formed in the roasting process.

4. *EXERCISE.* Mild exercise, particularly just after eating, shortens the emptying time of the meal. With strenuous exercise, gastric contractions are temporarily inhibited, then augmented, so that final emptying is not significantly delayed. Secretory activity does not appear to be materially influenced by exercise.

5. *POSITION.* In certain individuals, gastric emptying is facilitated when the position of the body is such that the pylorus and the duodenum are in a dependent position, i.e., with the individual lying on the right side. In the supine position, particularly in infants and in adults with a cascade stomach, the gastric content pools in the dependent fundic portion, and emptying is delayed. No evidence is available that secretion is affected by position.

6. *EMOTION.* The retarding effect of emotional states on gastric motility and secretion has been well documented by clinical and experimental observations. Evidence has been submitted (Wolf and Wolff) to indicate that the influence of emotions on gastric activity may be augmentative or inhibitory, depending on whether the emotional experience is of an aggressive (hostility, resentment) or depressive (sorrow, fear) type, respectively.

7. *PAIN.* Severe or sustained pain in any part of the body, e.g., kidney or gallbladder stone, migraine, sciatic neuritis, etc., inhibits gastric motility and evacuation by nervous reflex pathways.


Local (Gastric) Factors
Accelerating
Intermediate
Retarding
Tonicity of Stomach
Hypertonic stomach: empties most rapidly
Iliac crest
Orthotonic stomach: empties at intermediate rate
Hypotonic (or atonic) stomach: empties at slow rate
Character of Food
Starch: empties rapidly
Protein: empties at intermediate rate
Fat: empties slowly
Consistency of Food
Liquids: empty rapidly
Semisolids: empty at intermediate rate
Solids: empty slowly
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Motility of Small Intestine

The chyme, after its evacuation from the stomach, is propelled rather rapidly through the first and second portions of the duodenum. The rate of progression diminishes thereafter, as the intestinal contents are moved forward and are continuously mixed by an intricate combination of various types of muscular contractions. The complexity of the intestinal motility may be appreciated by watching a motion picture of the exposed intestine in an appropriately anesthetized, recently fed animal, or by observing the intestine covered only by skin in patients with a large ventral hernia. Tracings of intraluminal pressures confirm what is observed directly or by radioscopy, permitting the separation of three principal configurations. First can be recognized periods of simple low spikes occurring at a rate of up to 14 per minute in the jejunum and 8 to 10 per minute in the terminal ileum. These spikes are the expression of the continuously shifting annular constrictions of the lumen, by which intestinal segments are formed, divided, re-formed, redivided, etc. This type of activity, the *rhythmic segmentation* (upper right of figure on opposite page), serves to mix the chyme with the jejuno-ileal secretions and to expose and re-expose it to various areas of the mucosal surface for maximal absorption. These movements also exert a pumping action on the mucosal and submucosal blood and lymph vessels, thereby enhancing the transport of absorbed material into the circulation. The rhythmic segmentations give way to periods of higher and longer-lasting contractions, corresponding to the second type of intestinal movements, the *peristaltic waves* (center left), which (similar to the peristaltic waves of the esophagus, stomach, and duodenum) move the intestinal contents along to more distal parts of the gut, where the rhythmic segmentation is resumed. They are slower and more sluggish than the rhythmic segmentations and move the intraluminal food masses at a rate of 1 to 2 cm per minute. A third type of movement, a progression of waves in multiple intraluminal pressure recordings, is characterized by the more rapid passage of a contraction wave over a long segment of intestine. It is described as a *"peristaltic rush"* (center bottom) because, with such a contraction, the intraluminal contents move at speeds of from 2 to 25 cm per second. The forward movements are, to some extent, and particularly in the lower ileum, counteracted by *reverse peristalsis* (center)—antiperistaltic waves that cause a movement proximalward and serve to prolong the exposure of the contents to rhythmic segmentation. To these exteriorly visible movements must be added, finally, the *villous movements* (inset, upper left), which shorten the villi without changing the external diameter of the wall and are thought to aid absorption by expressing the contents of the epithelial cells into the veins and lacteals.

Intestinal peristalsis is brought about by the contraction of the muscularis propria, comprising the outer longitudinal and inner circular layers, forming a continuous tube that lengthens, shortens, twists, and constricts so that the enclosed contents are constantly agitated and propelled for shorter or longer distances until the remnants are driven out completely. It takes from 3 to 5 hours after ingestion of a mixed meal for the "head" of the intestinal column to reach the cecum, by which time the stomach is usually empty. The entire meal traverses the small intestine in 5 hours, a period that is shortened by the intake of another meal. Progress of the intestinal contents, owing to a more active peristalsis in the proximal parts, is more rapid through the jejunum than through the ileum.

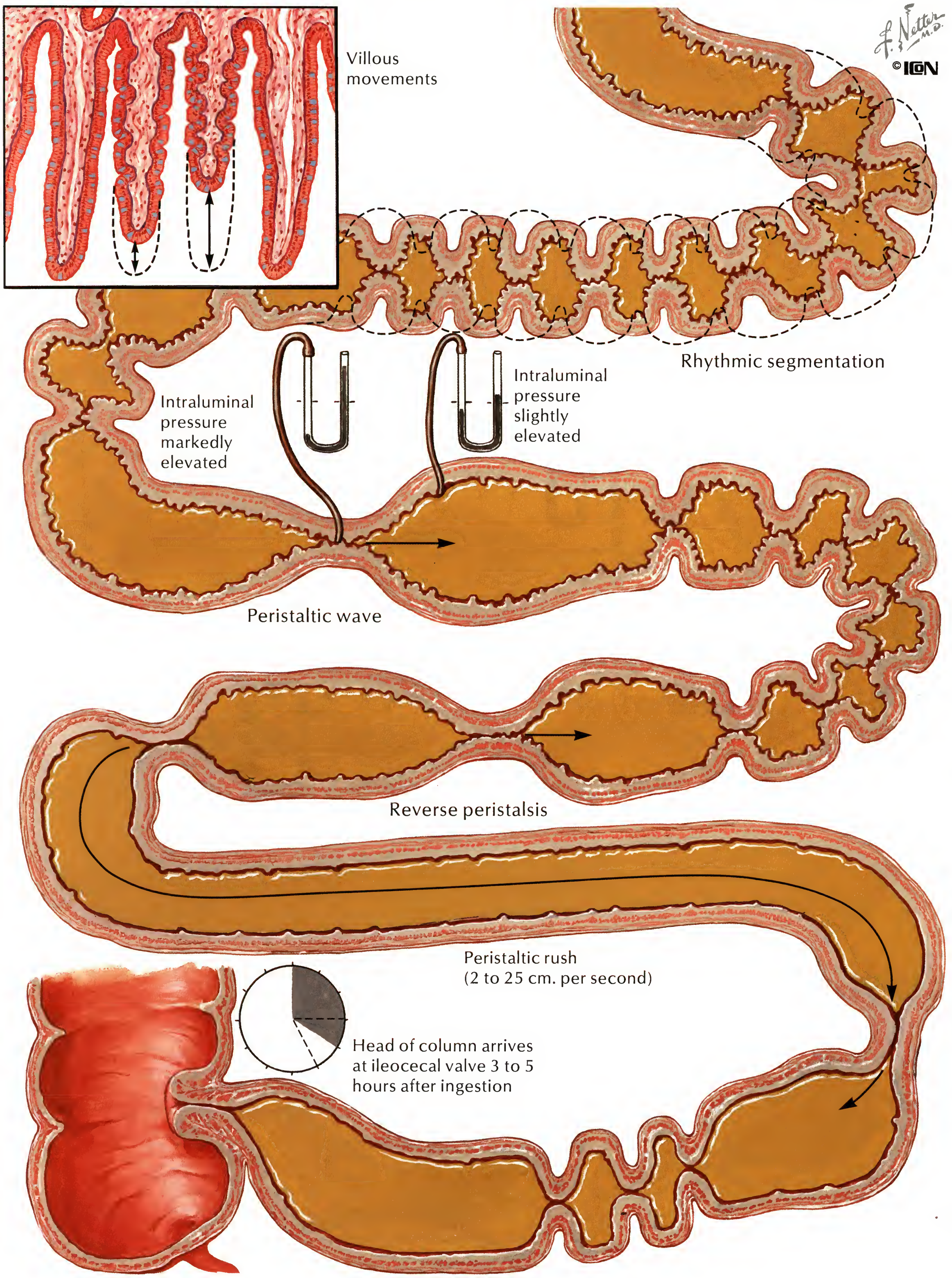
The mechanism of peristalsis has been the subject of considerable investigation and speculation. From early experiments (Bayliss and Starling, 1899) it was concluded that the propagation of the peristaltic wave along the gut depends upon a contraction above and a relaxation below any point of excitation. This is known as the "law of the intestine" or the "myenteric reflex." Others have suggested that the segment immediately caudad to the point or zone of contraction is not "relaxing," but that, distad to the segment in which both the longitudinal and the circular muscle layer contract, the longitudinal fibers alone contract, effecting a shortening and enlarging of the lumen. This would mean that the myenteric reflex involves differential contractile phases of the respective muscular components rather that a contraction-relaxation cycle, as the "law of the intestine" has postulated.

Another theory (Alvarez, 1928) ascribed the orderly progression of peristalsis to a number of gradients, which are defined as gradations in certain attributes, properties, or biologic characteristics of the gut from the duodenum downward. The rate of rhythmic contractions, the propulsive force, tonus, resistance to distention and to the digestive action of gastric juice, secretory activity, oxygen consumption, carbon dioxide production, lactic acid, acetylcholine and catalase content, responsiveness to histamine—all these and many other indices of biologic activity, diminishing from above downward, comprise the *"gradients"* that, according to this theory, govern the transfer of material from the stomach to the colon.

The integrated actions of the muscular apparatus of the intestines must derive from intrinsic properties. Support can be seen in the behavior of a loop of intestine that has been isolated, turned on its mesentery, and re-anastomosed in reverse, as indicated in the illustration. The peristalsis persists in the original direction; i.e., the peristaltic waves in the "turned" loop are opposite to the main peristaltic stream.

Ileocecal Sphincter

The junction of the small intestine with the colon is sometimes referred to as the ileocecal valve, partly because of its structural appearance in some anatomic specimens and partly because the end of the ileum, being wedged into the wall of the colon, seems to function, in some individuals, in the manner of a flutter valve. Observations on the living individual (Di Dio) indicate, however, that the ileocecal junction functions as a true sphincter, meaning that it regulates the flow of material from the ileum to the cecum, as well as prevents its retrograde passage. Thus the contact of the intestinal contents with the terminal ileal mucosa is prolonged, favoring maximal intestinal absorption. The sphincter opens when a peristaltic wave, passing along the terminal ileum, builds up enough pressure to overcome the resistance of the sphincter. The cecum at first manifests receptive relaxation. Increasing pressure in the cecum, either by overdistention or by a peristaltic contraction, causes a reflex contraction of the sphincter, preventing overfilling of the cecum and ceco-ileal reflux. Frequently, material introduced by enema is observed to pass into the small intestine, probably owing to a functional incompetence of the sphincter or its reflex regulation. The significance of this sphincter mechanism in protecting the ileum from the reflux of cecal contents remains somewhat conjectural.


Villous
movements
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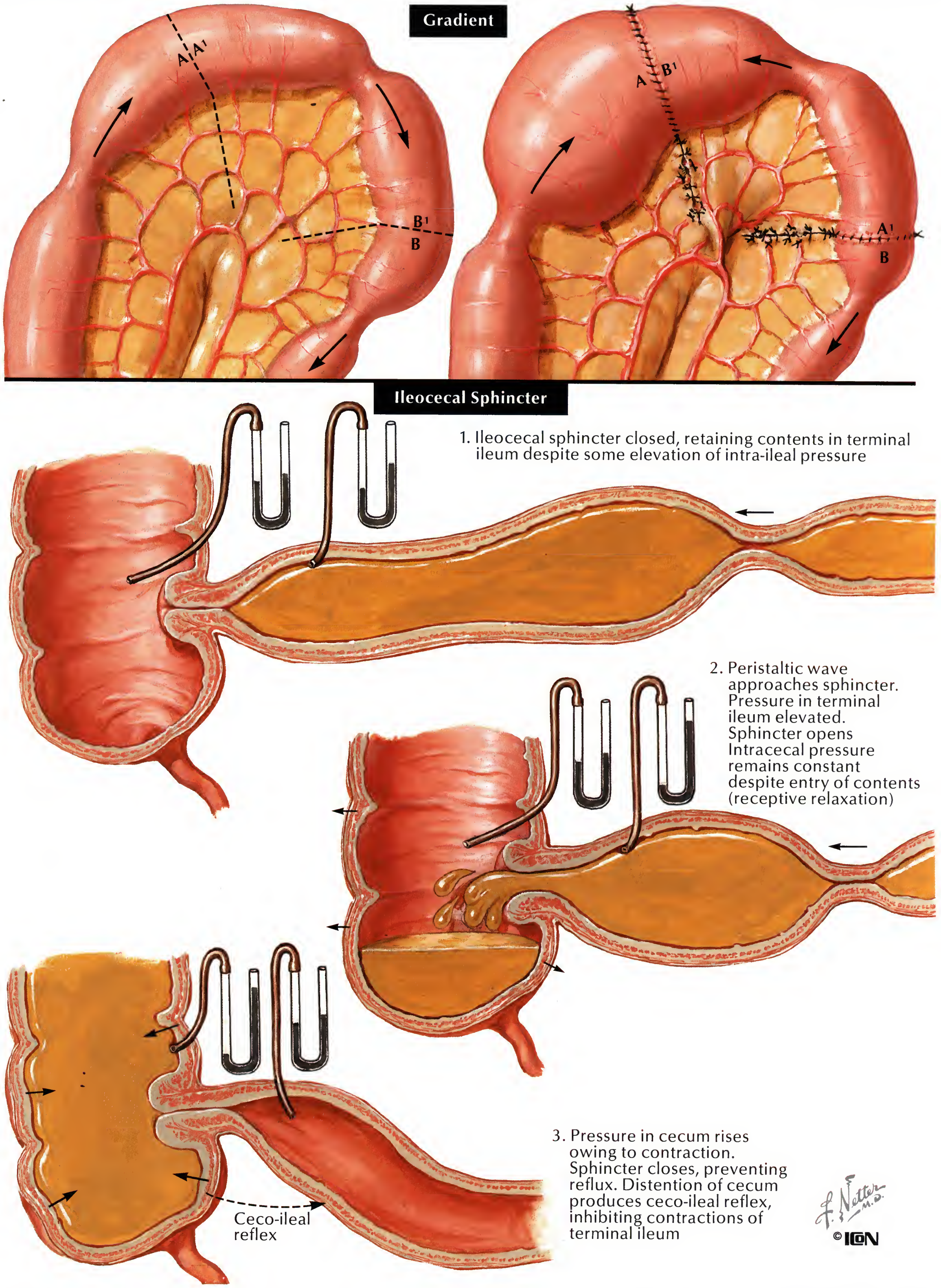
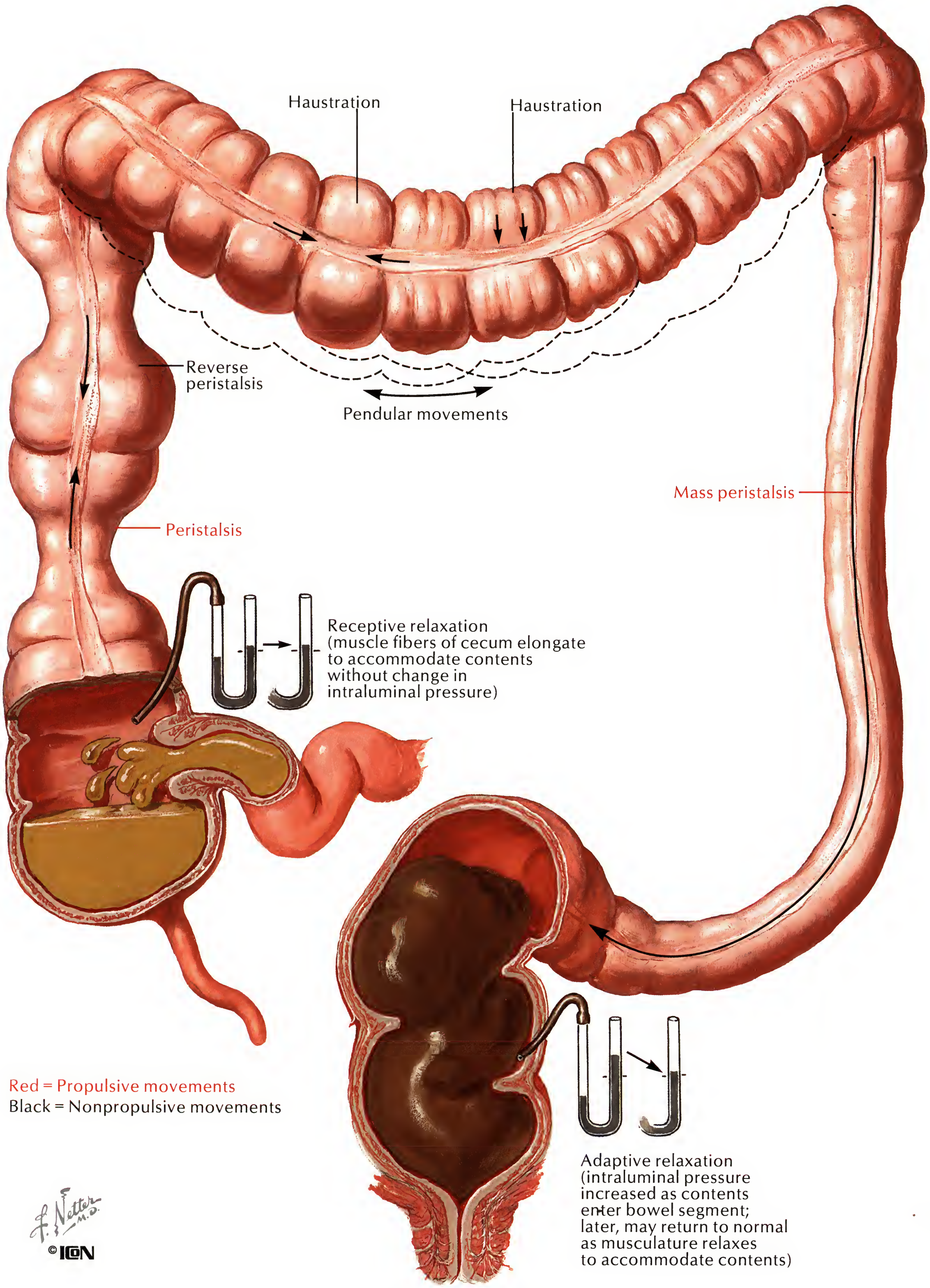
Rhythmic segmentation
Intraluminal
pressure
markedly
elevated
Intraluminal
pressure
slightly
elevated
Peristaltic wave
Reverse peristalsis
Peristaltic rush
(2 to 25 cm. per second)
Head of column arrives
at ileocecal valve 3 to 5
hours after ingestion

Motility of Small Intestine (continued)




Haustration
Haustration
Reverse peristalsis
Pendular movements
Mass peristalsis
Peristalsis
Receptive relaxation (muscle fibers of cecum elongate to accommodate contents without change in intraluminal pressure)
Adaptive relaxation (intraluminal pressure increased as contents enter bowel segment; later, may return to normal as musculature relaxes to accommodate contents)
Red = Propulsive movements
Black = Nonpropulsive movements
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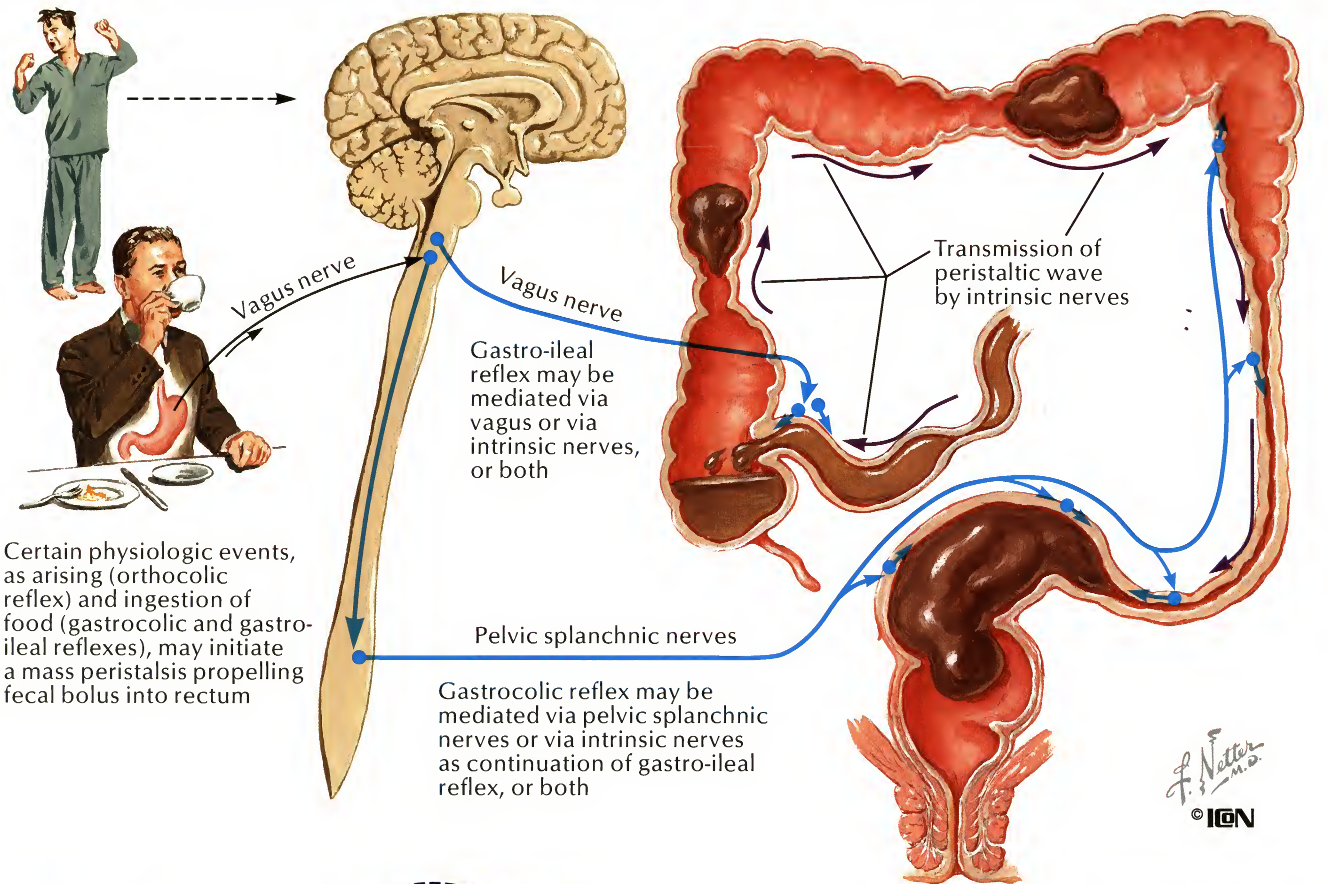
Motility of Large Intestine (continued)

As with the small intestine, various types of colonic movements can be differentiated. The *receptive relaxation* of the cecal musculature, as the terminal ileum evacuates its content, permits the accommodation of adequate quantities of the intestinal chyme before the activation of stretch receptors. The *adaptive relaxation* in other parts of the colon provides, similarly, accom-modation of the fecal content without distress and without premature propulsion, as, e.g., in the rectum when, for one reason or another, defecation is deferred. Such a "reservoir continence" function is a property particularly of the descending colon, and it is this feature that renders a colostomy a fairly tolerable and practical condition. *Contraction* of the *longitudinal muscular bands* (*taeniae*) shortens the bowel and forms pleats or sacculations (haustra) in which the residues of the chyme are retained to allow time for the absorption of water and a number of digestion products. This function is abetted by *contractions of the circular muscle*, which may create small indentations within the haustra. These contractions of the longitudinal and circular musculature may be considered processes analogous to the rhythmic segmentations of the small bowel. Pendular movements—a slow, swinging motion of the transverse colon— probably are brought about by changes in the tonus of the longitudinal muscles, and antiperistalsis, or retrograde movements, occur, to some extent, particularly in the right colon, but they are less typical there than in other parts of the intestinal tract. To these *nonpropulsive movements* must be added the *propulsive peristalsis*, which consists of (1) slow irregular contractions, which arise in a proximal segment and pass in a caudad direction for a short distance, obliterating a few haustra, and (2) the *mass peristalsis*, an analogue to the peristaltic rush of the jejunum or ileum. The mass peristalsis, occurring only two to three times in 24 hours and initiated principally by the gastrocolic reflex, propels the colonic contents toward the rectosigmoid by contractions that involve a broad segment of the colon.

In a study of the complex distribution of the autonomic innervation of the colon, it should be kept in mind that in the colon the distribution is extremely variable, particularly in the vicinity of the splenic flexure. The extrinsic nerves exert only a regulating effect on the intrinsic nerve network of the colon, which functions autonomously and is capable of coordinating movements of adjacent segments necessary for peristaltic progression, except in a variety of pathologic conditions.

The concept that the parasympathetics (cholinergic nerves) generally augment and the sympathetics (adrenergics) inhibit muscular contraction is acceptable as a convenient working hypothesis to formulate roughly the nature of the functional disturbances of the large bowel, provided it is understood that the net effect of stimuli reaching the colon from either component of the autonomic system is a resultant not only of the extrinsic stimuli, but also of the reactivity of the intrinsic nerves, the degree of muscular excitation, and other local conditions of the colon. Thus, depending upon the given situation, either cholinergic or adrenergic impulses may stimulate, on other occasions may inhibit, and on still others may mediate opposite effects simultaneously on different parts of the colon.



Vagus nerve
Vagus nerve
Transmission of peristaltic wave by intrinsic nerves
Gastro-ileal reflex may be mediated via vagus or via intrinsic nerves, or both
Certain physiologic events, as arising (orthocolic reflex) and ingestion of food (gastrocolic and gastro-ileal reflexes), may initiate a mass peristalsis propelling fecal bolus into rectum
Pelvic splanchnic nerves
Gastrocolic reflex may be mediated via pelvic splanchnic nerves or via intrinsic nerves as continuation of gastro-ileal reflex, or both
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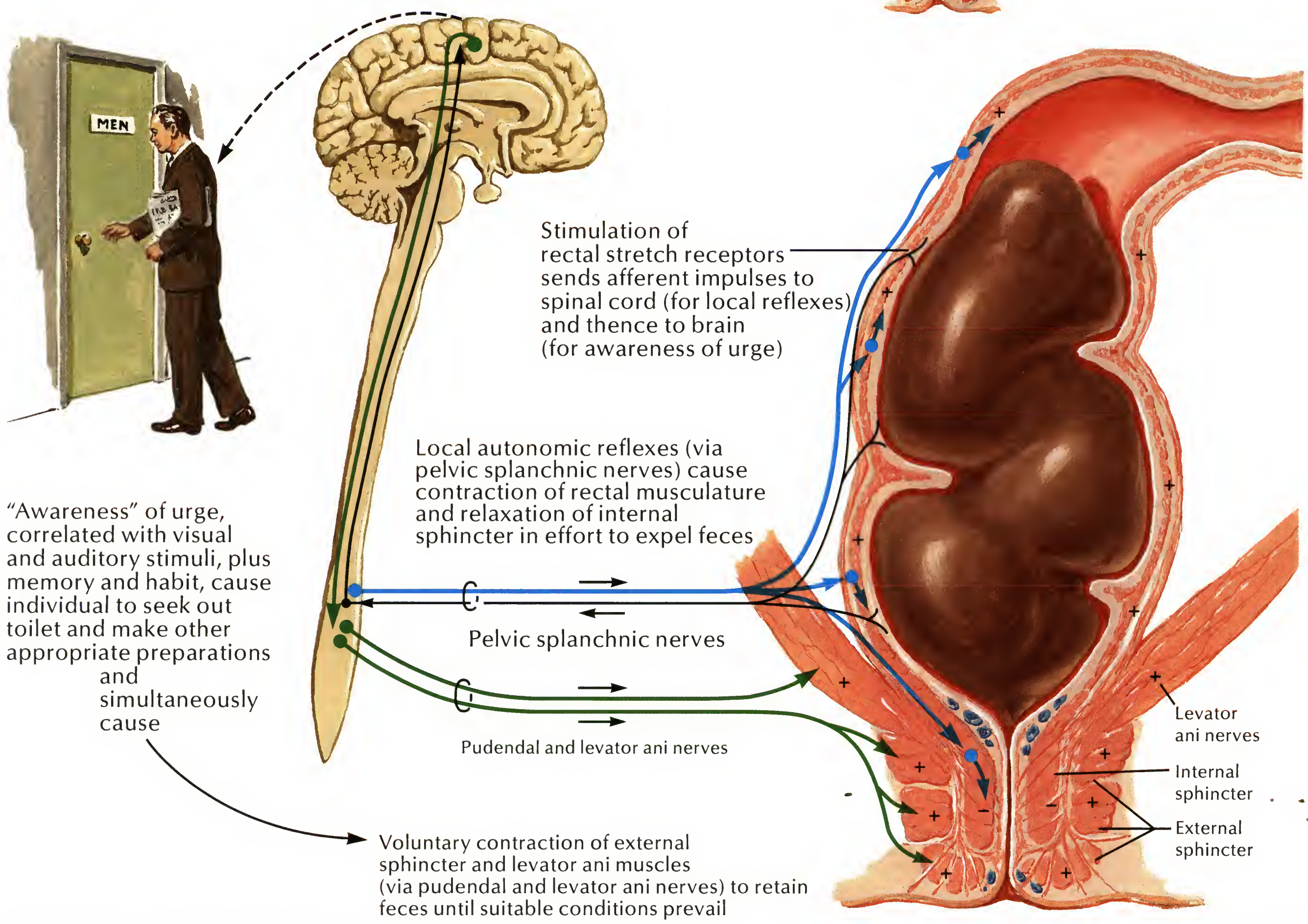


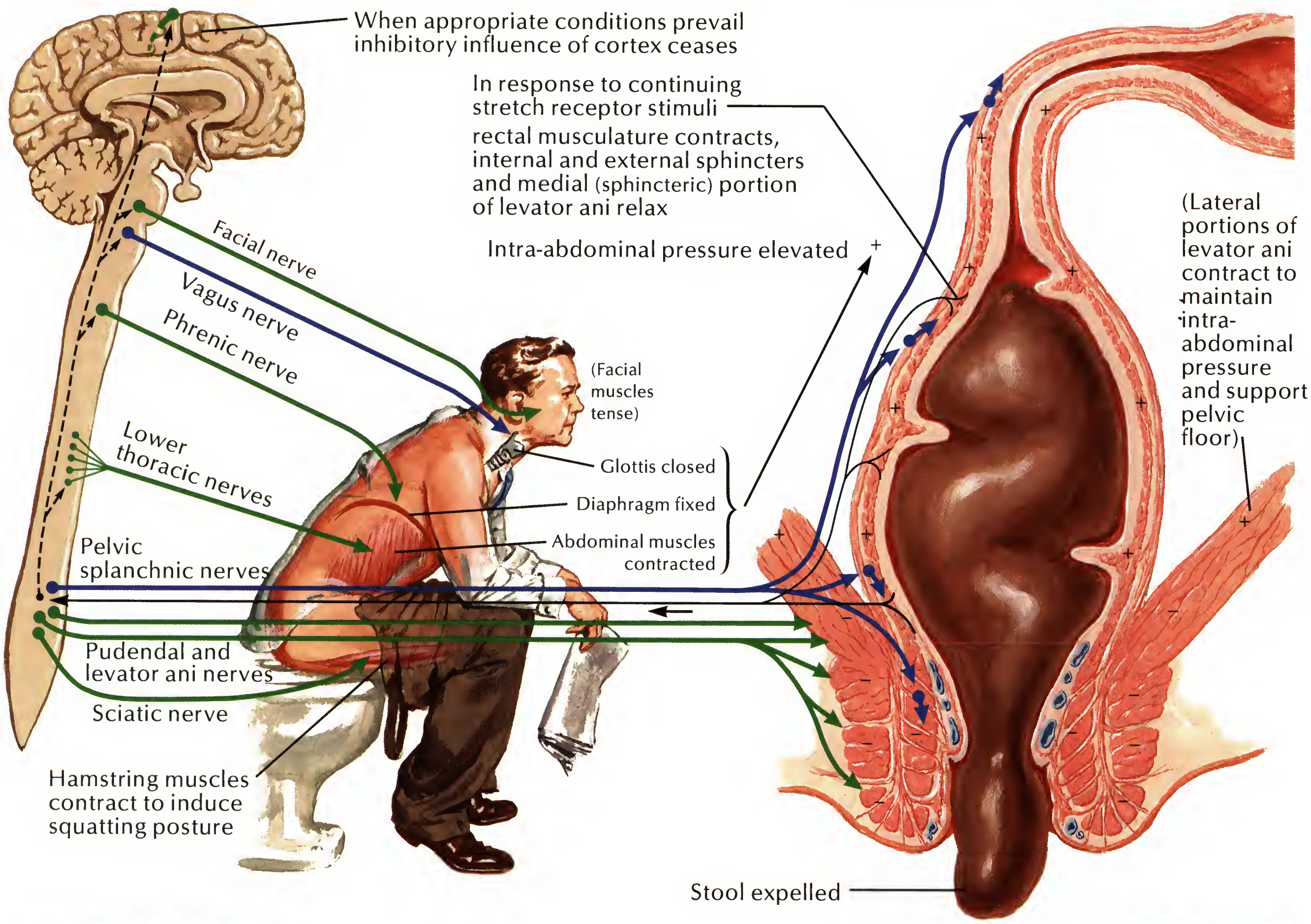
MEN
Stimulation of rectal stretch receptors sends afferent impulses to spinal cord (for local reflexes) and thence to brain (for awareness of urge)
Local autonomic reflexes (via pelvic splanchnic nerves) cause contraction of rectal musculature and relaxation of internal sphincter in effort to expel feces
"Awareness" of urge, correlated with visual and auditory stimuli, plus memory and habit, cause individual to seek out toilet and make other appropriate preparations and simultaneously cause
Pelvic splanchnic nerves
Pudendal and levator ani nerves
Voluntary contraction of external sphincter and levator ani muscles (via pudendal and levator ani nerves) to retain feces until suitable conditions prevail
Levator ani nerves
Internal sphincter
External sphincter

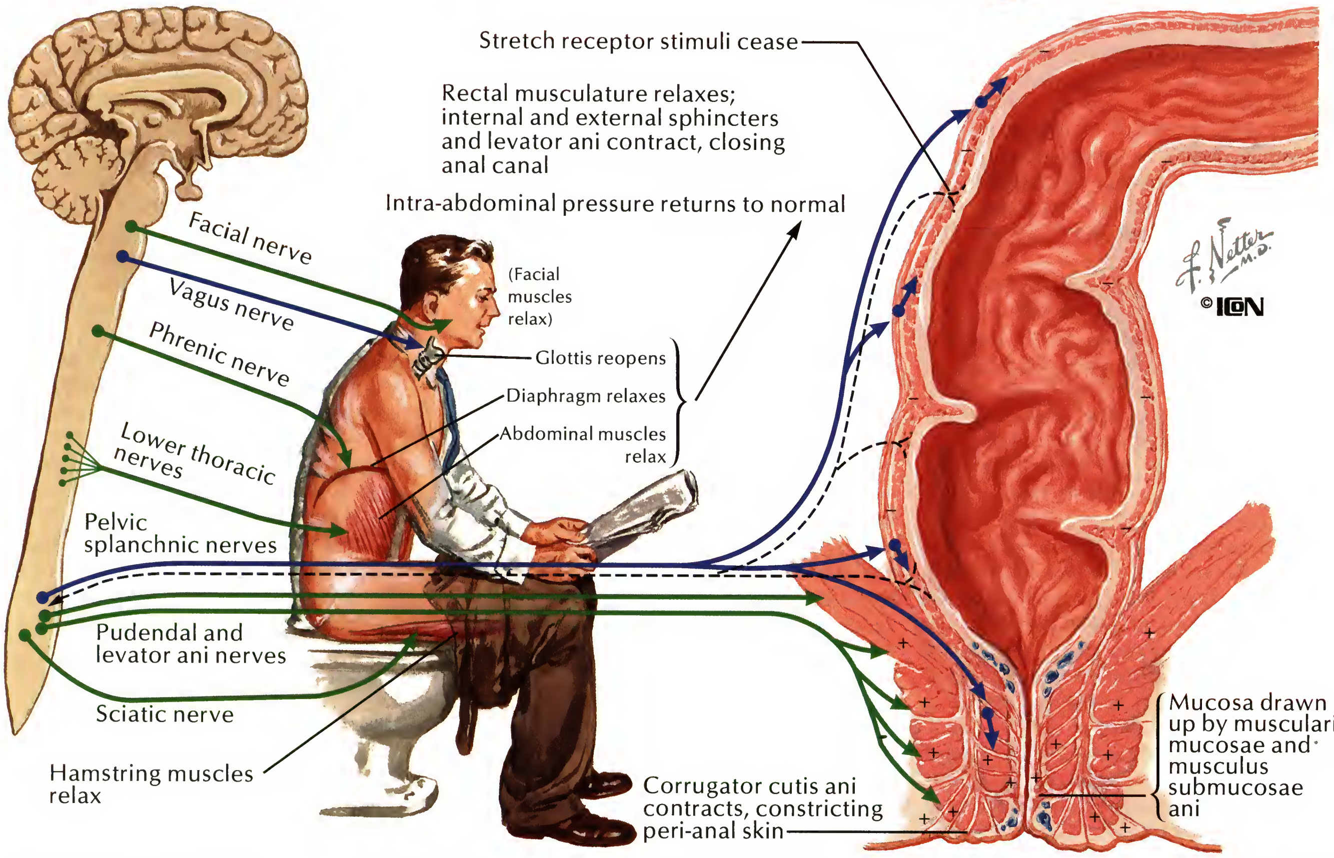
The mechanisms operating in the process of egestion of the alimentary residues are, in several respects, counterparts of those governing ingestion, particularly deglutition. Both functions involve simultaneous actions of voluntary and involuntary muscles, both are highly susceptible to derangement by emotional stimuli, and both, though to a degree capable of autonomous regulation by intrinsic nerves, are seriously impaired by complete extrinsic denervation. Cerebral influences on defecation are exerted by neurons of the motor cortex, which permit the voluntary contraction of the external anal sphincter, the levator ani muscle, and the musculature of the abdominal wall. A center in the midbrain has been shown to affect the tonus of the muscles of the rectum, and a medullary center in the floor of the fourth ventricle, after appropriate stimulation, appears to give rise to straining and the evacuation of stool. This center presumably involves autonomic fibers en route from the hypothalamus to the spinal cord to reach the distal third of the colon and the anorectal structures via the autonomic outflow. Sympathetic impulses (via inferior mesenteric ganglia, hypogastric nerves, and inferior hypogastric [pelvic] plexus) tend to exert an inhibitory effect on the rectal muscles and a variable one on the internal anal sphincter. Primarily responsible for the contraction of the rectum and the relaxation of the sphincter—and thus for the coordinated act of defecation—is the parasympathetic nerve center in the sacral segments of the spinal cord (a counterpart of the cranial centers regulating deglutition). The intrinsic nerve network, well developed in the anorectal region, coordinates the movements of adjacent parts of the anorectal segment and confers some degree of autonomy of action, independent of the extrinsic innervation. It is, moreover, significant that the voluntary nerve supply to the external sphincter and the levator ani (pudendal nerve) originates from the same spinal segments from which the pelvic splanchnics derive; this arrangement facilitates the reflex integration of the action of the sphincter and rectal muscles.

Of the many reflex mechanisms involved in the complex act of defecation, the following are manifestly of practical importance. Visual, auditory, or olfactory receptors may inhibit or stimulate the rectum via the cerebral cortex, spinal autonomic pathways, and lumbar or sacral autonomic nerves. Stretch receptors in the rectal mucosa may, via afferents to the spinal cord, influence the external sphincter and muscles involved in squatting, bearing down, straining, and supporting the pelvic floor. Receptors in the anal canal and external sphincter send stimuli, via somatic afferents, to sacral segments of the spinal cord to increase, via autonomic outflow, the contraction of the rectal muscles when fecal masses are passing through the canal. Another reflex from rectum and sphincters through afferents to the sacral centers acts, via the autonomic outflow, to arrest micturition when defecation occurs. From receptors in the perianal skin, a reflex stimulates rectal contraction and transient contraction of the external sphincter and levator muscles via the sacral center. When the nerve terminals of the rectal mucosa are stimulated by distention, sensory impulses pass, via visceral afferents, through the dorsal root ganglia to the respective spinal segments, whence they are distributed by at least three routes. The first goes via *ascending tracts to the sensory cortex* to engender awareness of the urge to defecate and to bring forth all the necessary voluntary actions connected with the discharge of fecal matter. The second impulse passes via connector neurons from dorsal to ventral horn cells to mediate reflex relaxation of the external sphincter and reflex contractions of the abdominal, perineal, and hamstring muscles. The third reaches the lateral column cells, synapsing with neurons of the pelvic autonomous nerves and stimulating the longitudinal and circular rectal musculature for the coordinated action that drives the fecal mass toward and through the anus.

A mass peristalsis moving the content of the left colon into the rectum may be considered to constitute the initial phenomenon of the sequence of events in defecation. The urge to defecate ordinarily occurs when the residues accumulate in the rectum; this happens at intervals varying from several times in one day to every fourth or fifth day. The majority of people feel this urge once daily, usually in the morning after breakfast, when awakening from sleep, assuming the erect position (*orthocolic reflex*), moving about, and, particularly, ingesting food and liquids (*gastrocolic reflex*) favor the initiation of a mass peristalsis. Increased intrarectal pressure brings about a reciprocal relaxation of the anal sphincters, which, however, is counteracted by *voluntary contraction of the external sphincter*, which permits delay of defecation until circumstances permit the act to proceed. If the delay is prolonged, a temporary reduction in the intensity of the urge may ensue. These adjustments are a manifestation of the property of adaptive relaxation, i.e., the ability of the rectal musculature to adapt itself to continued distention by a reduction in the force of its contraction.

The urge, i.e., the awareness of the need to evacuate the rectum, is responded to, under natural conditions, with a minimum of delay. The individual assumes a *squatting position*, which is facilitated by a reflex *contraction of the hamstrings*, one of those reflex mechanisms not yet developed in the newborn but acquired within the first 24 months of life. The squatting position supports the increase in the intra-abdominal pressure, which is accomplished by *contraction* and *fixation of the diaphragm*, *closure of the glottis*, and *contraction of the muscles of the abdominal wall*. The voluntary controlled contraction of the external sphincter is released, and the fecal mass is expelled by the increasing rectal contraction, which leads to intrarectal pressure of 100 to 200 mm Hg (Hurst). Simultaneously, the muscles of the pelvic floor contract, contributing to the forces that increase the intra-abdominal pressure but also acting to prevent the anus from being forced too far downward with the emerging fecal bolus. The content of the left colon, or part of it, may be emptied in a single, continuous peristaltic progression, or the anorectal structures may return to the resting state after the first bolus has been evacuated, until another contraction of the colon delivers more material into the rectum to set the sequence of events into action again.


When appropriate conditions prevail
inhibitory influence of cortex ceases
In response to continuing
stretch receptor stimuli
rectal musculature contracts,
internal and external sphincters
and medial (sphincteric) portion
of levator ani relax
Intra-abdominal pressure elevated
(Lateral
portions of
levator ani
contract to
maintain
intra-
abdominal
pressure
and support
pelvic
floor)
Facial nerve
Vagus nerve
Phrenic nerve
Lower
thoracic nerves
Pelvic
splanchnic nerves
Pudendal and
levator ani nerves
Sciatic nerve
Hamstring muscles
contract to induce
squatting posture
(Facial
muscles
tense)
Glottis closed
Diaphragm fixed
Abdominal muscles
contracted
Stool expelled


Stretch receptor stimuli cease
Rectal musculature relaxes;
internal and external sphincters
and levator ani contract, closing
anal canal
Intra-abdominal pressure returns to normal
Facial nerve
Vagus nerve
Phrenic nerve
Lower thoracic
nerves
Pelvic
splanchnic nerves
Pudendal and
levator ani nerves
Sciatic nerve
Hamstring muscles
relax
(Facial
muscles
relax)
Glottis reopens
Diaphragm relaxes
Abdominal muscles
relax
Corrugator cutis ani
contracts, constricting
peri-anal skin
Mucosa drawn
up by muscularis
mucosae and
musculus
submucosae
ani
F. Netter M.D.
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Secretory, Digestive, and Absorptive Functions of Small and Large Intestine

The mucosa of the gut throughout its entire length is equipped with secretory cells. The secretory product of the duodenal glands is an alkaline, pale-yellow, viscous fluid, consisting essentially of mucus, the primary function of which appears to be the protection of the proximal duodenum against the corrosive action of the gastric chyme. The glandular apparatus of the jejunum and ileum produces the succus entericus, the importance of which, in the normal digestive process, is difficult to assess in view of its being constantly mixed with bile and pancreatic juice. The intestinal secretion contains mucus as well as enzymes, namely, *peptidases*, *nucleases*, *nucleosidases*, *phosphatase*, *lipase*, *maltase*, *sucrase*, *lactase*, and the coenzyme enterokinase, which activates trypsinogen and chymotrypsinogen of pancreatic origin to trypsin and chymotrypsin, respectively. Under normal conditions, the succus entericus has a protective, diluting, and lubricating function rather than a digestive one. Its flow is stimulated by the presence of acid reaction in the upper intestine; by local mechanical and chemical stimuli; by administration of secretin, enterocrinin, and pilocarpine; and by sympathectomy.

The mucus membrane of the colon, when stimulated mechanically or chemically, secretes an opalescent, alkaline fluid composed of water, mucus, and, possibly, some enzymes.

Digestion

The *intestinal digestion of proteins* is carried out by an array of enzymes, deriving partly from the intestinal glandular apparatus but primarily from the pancreas. The proteolytic action of the succus entericus, previously ascribed to a single entity called erepsin, depends upon a number of protein-splitting enzymes, each with a highly specific effect. Each one attacks only certain linkages of the protein molecule or of the degradation products resulting from the preceding effects of one or more catalytically active compounds. Similar to the specific activities of *trypsin*, *chymotrypsin*, and carboxypeptidase, the intestinal *aminopeptidase* acts only upon *polypeptides* or *peptides* containing a free amino group, liberating amino acids by scission; the *dipeptidase* acts only upon dipeptides, etc., until the original protein has been completely fragmented to its elementary components, the twenty-odd *amino acids*.

For the *digestion of nucleoproteins*, the pancreas supplies nucleases, ribonuclease, desoxyribonuclease, and others that specifically hydrolyze nucleosides (pentose or desoxypentose conjugated to bases such as purines and pyrimidines). The intestinal secretion also provides nucleases and, particularly, phosphatases, which split nucleotides (phosphoric esters of nucleosides) into their components.

The processes involved in the *digestion of carbohydrates* consist generally of an enzymatic cleavage of poly- and oligosaccharides into monosaccharides. In human nutrition the most important carbohydrate is *starch*, which is a polysaccharide occurring as an energy reservoir in plants, particularly cereals, grains, roots, tubers, etc. The counterpart in animals is glycogen, another polysaccharide ingested with meat and liver. In both starch and glycogen, a large number of hexoses (monosaccharides) are linked together, forming either a straight or a branched chain of molecules. The linkage between these molecules varies, and, to open them, the organism is equipped with a variety of specifically active enzymes. The starch-splitting enzymes, called amylases, are secreted by the salivary glands and the pancreas. The action of the amylases yields the disaccharide *maltose* and a polysaccharide fragment called *dextrin*, which is not attacked by amylase. The activity of the salivary amylase, known as ptyalin, is exerted mainly in the inner portions of the food mass in the stomach before the gastric juice has sufficiently penetrated it, but fails to penetrate the granules of uncooked starch. The more effective enzymes are the pancreatic amylases (two distinct types, the α- and β-amylase, have been recognized). Thus, except during the period of infancy, when the secretory activity of the pancreas has not yet fully developed, the degradation of starch into the disaccharide maltose and the monosaccharide *glucose* is completed in the lower part of the duodenum and in the jejunum and ileum. The splitting of maltose into two molecules of glucose is catalyzed by *maltase*, an enzyme formed by the intestinal glands. Other intestinal enzymes are *sucrase* (invertase) and *lactase*, which convert sucrose (our common kitchen sugar) into a molecule of glucose and *fructose*, or lactose (mild sugar) into glucose and *galactose*, respectively. The end products, thus, are simple hexose units, which the intestinal epithelial cell is prepared to absorb (see below). In the human, cellulose is indigestible because humans, in contrast to some animals, lack enzymes capable of attacking the specific bonds of cellulose. Some exo-enzymes deriving from the bacterial flora of the human colon may act upon cellulose and upon the small amount of undigested starch reaching the distal gut.

The normal diet of humans contains a considerable amount of substances that, in contrast to carbohydrates and proteins, are soluble not in water, but only in the so-called "fat solvents" (ether, chloroform, benzene, and many others). This group of compounds, which includes entities of quite heterogenous structure, is classified as "*lipids*." The term includes neutral fat, phosphatides, cerebrosides, steroids, and fat-soluble vitamins. From the dietary point of view, the neutral fats are of major importance, mostly on account of their high energy value. Neutral fats, whether of plant or animal origin, are esters of glycerol and fatty acids. These esters are called *triglycerides*, because the three alcoholic hydroxyl groups of glycerol are bound in an ester linkage to the carboxyl group (the group that determines the acid character) of either saturated or unsaturated organic acids, such as palmitic, stearic, oleic, or linoleic. The *neutral fat* (neutral because no acidic group is free) is *digested* by hydrolyzation of the ester linkage, yielding the components of the esters, namely, *glycerol* and various *fatty acids*. Evidence has been offered that some fat molecules may escape digestion and be absorbed unchanged (see below) and that the splitting of fat occurs in stages, meaning that the *triglycerides* lose first one of the three acid molecules, leaving a *diglyceride* (i.e., a glycerol ester containing only two acids), and this, in turn, is hydrolyzed to a *monoglyceride*, which possesses only one acid molecule. Thus, the digestion of fat furnishes a multiplicity of split products, the ratio of which, in the intestinal lumen, varies to a great extent.

The hydrolysis of fat is accomplished by active substances called *lipases*, which are secreted by the pancreas and to a much lesser extent by the intestinal glands. A negligible amount of fat may be digested in the stomach by a lipase of gastric origin, which, in contrast to other lipases, acts in a nearly neutral environment. In adult life this gastric lipase is of no practical significance, but it may play a role in infancy and may be capable of hydrolyzing the highly emulsified fat of the milk. The bulk of fat in the adult diet is digested by the pancreatic lipase. In the lower duodenum the fat is mixed with bile and dispersed into a fine emulsion. The components of bile responsible for this action are the bile acids, mostly glycocholic and taurocholic acid, which are most powerful detergents. The result of the emulsification of fat in the aqueous

medium of the intestinal chyme is an enormous increase of the surface of the fat particles, facilitating the hydrolytic action of the pancreatic and intestinal lipases. In contrast to the enzymes involved in protein and carbohydrate digestion, which act with a high degree of specificity upon certain compounds or chemically well-defined groups or bonds, the action of lipases of animal or plant origin is far less specific. Being esterases, they act exclusively upon esters. It is, however, characteristic of the lipases (as of all esterases) that they not only catalyze the hydrolysis of esters, but also cause the opposite reaction, namely, the synthesis of esters. In other words, the splitting of an ester by lipase is an easily reversible action. Hydrolysis and esterification can proceed simultaneously, the rate of the two reactions depending on an equilibrium (between substrate, enzyme, the substrate-enzyme complex, and the reaction products), which has been well studied in vitro but, owing to its complexity, not in vivo. At any rate, this feature of lipase activity obviously contributes to the constant presence of tri-, di-, and monoglycerides, glycerol, and fatty acids in the intestinal chyme.

The fatty acids, whether ingested with the food or arising as split products of fat hydrolysis, combine in the intestine with cations, forming soluble soaps with Na and K and insoluble soaps with Ca and Mg. The soluble alkali soaps aid in the emulsification of fat and the stabilization of emulsified lipids by the same principle that makes soap useful in the household for cleansing and detergent effects. The formation of insoluble soaps represents also a sort of regulating mechanism insofar as it withdraws the fatty acids from the reaction mixture of enzymes, fat, and its split products.

Other lipids, such as vitamin A (and its provitamin carotene), vitamins E and K_1, and the steroids, including cholesterol and vitamin D, are not broken down within the intestine. The phospholipids (phosphatides) may remain in part unchanged, and in part are hydrolyzed into their components, viz., glycerol, fatty acids, phosphate, and the special compound characteristic of the particular phospholipid (choline, serine, inositol, or ethanolamine). The pancreatic juice contains a specific lecithinase that liberates isolecithin, a compound said to aid in the emulsification of dietary fat.

Absorption

The purpose of the complex enzymatic reactions to which foodstuffs are exposed within the intestinal lumen is to prepare the nutrients for transfer into and assimilation within the organism. The lumen, i.e., the space encompassed by the wall of the digestive tube, belongs, fundamentally speaking, to the outside world, and the process, or processes, by which the products of digestion enter and pass through the intestinal wall into the circulation is called absorption. The site of absorption is almost exclusively the duodenal, jejunal, and ileal surface epithelium, although it is known that some absorption may take place in the colon (see below) and that both the oral and gastric mucosae are able to absorb some material. The epithelial lining of the small intestine is preeminently and specifically equipped for its function by its length and its large surface area. The mechanisms involved in the absorptive process, though they have been studied during many past decades, have by no means been completely elucidated. The sole fact that several substances are absorbed against a concentration gradient is proof that specific cellular activities are necessary to make absorption possible, so to speak, against the physical rules that govern diffusion and osmosis. It is impossible to describe absorption in general terms, not only because our knowledge of it is fragmentary, and to a great extent still controversial, but also because, for almost every single substance offered for absorption, a different mechanism or a different pathway is employed.

Water crosses the intestinal wall in both directions, depending essentially upon the concentration of solutes in the chyme. If the aqueous phase of the intestinal contents is hypotonic, water moves from the lumen through the cells, or, possibly, between the cells through pericellular spaces into the blood (Visscher). Vice versa, if the chyme is hypertonic, water will be transferred from the blood into the lumen. As crystalloid solutes enter the wall, an obligatory transport of water from the lumen occurs to keep the solution within the tube from becoming too hypotonic. It has been suggested that the movements of water to and from the intestinal wall are regulated by osmotic forces.

A great part of the minerals, such as the salts composed of sodium, potassium, and chloride ions, moves with the water, but, in addition, some specific processes must be inferred to explain the selective absorption of chlorides in the presence of sulfates or the absorption of NaCl against a steep concentration gradient (Jacobs). The optimal absorption of calcium ensues under conditions of proper pH, with an adequate supply of bile, in the presence of a favorable ratio of digestible fat, and in the absence of those substances that, like oxalic or phytic acid, form insoluble calcium salts. The fact that diversion of bile from the intestine diminishes, and stimulation of bile flow increases, the absorption of calcium suggests that calcium may be transferred into and through the cells in combination with bile acids. Large amounts of lactose (or galactose) improve the conditions of calcium absorption, especially in children, owing to the presence in the gut of lactobacilli, which ferment lactose to lactic acid, which, in turn, acidifying the intestinal contents, increases the solubility of calcium phosphate. Strong evidence is available to indicate that vitamin D mediates calcium absorption. Little is known about the conditions and processes involved in the absorption of magnesium, which probably follows much the same lines as calcium. Phosphorus in the intestine, predominantly present in the form of orthophosphate, is presumably transported after esterification at the cell surface.

The products of protein digestion, the amino acids, are apparently absorbed as promptly as they are split off from the proteins. The mechanism by which the transfer is accomplished is obscure, but it clearly involves more than simple diffusion or osmotic movement through the cell. The rate of absorption for various amino acids is different. With the exception of tryptophan, leucine, isoleucine, valine, and alanine, the L-isomers are more readily transferred than are the D-isomers. By far the greater part of the amino acids enter the circulation via the portal vein; only a small amount may leave the intestine by way of the lymphatics. Significant quantities of peptides, either entering the cells or synthesized within them, reach the circulation, as indicated by a rise of peptide nitrogen in the blood. Under special circumstances, e.g., when proteolytic enzymes are inadequately secreted or when, for unknown reasons, as in many allergic conditions, the barrier function of the epithelial lining is disturbed, intact protein molecules may be absorbed.

Carbohydrates are *absorbed* almost exclusively in the form of monosaccharides, i.e., as hexoses (glucose, fructose, and galactose) or pentoses (ribose, arabinose). The absorption of small amounts of disaccharides (sucrose and lactose) has been demonstrated, but is of no practical significance. Galactose is more rapidly absorbed than is glucose, and glucose more rapidly than is fructose. Within fairly wide limits, the rate of hexose transfer is independent of the concentration in the chyme. From the differences in the rate of absorption of

the hexoses, which should diffuse with the same speed; from the fact that one and the same hexose is more readily absorbed in the form of its dextrorotatory stereoisomer than it is absorbed as a levorotatory stereoisomer; and from the fact that pentoses, in spite of their smaller molecular structure, actually need more time to pass through the wall, it must be concluded that the transport of these simple sugars involves more than diffusion and selective, active processes are clearly involved. The presence of enzymes (hexokinases) catalyzing the conversion of hexoses to hexose phosphates in the intestinal mucosa and the reduction of glucose and galactose absorption when the hexokinases are inhibited by phlorizin suggest the possibility that a *phosphorylation* mechanism is the active process in sugar absorption. Other evidences, however, are not in harmony with such an assumption. The picture of the absorption of pentoses is still less clear. The transfer of xylose may involve diffusion or phosphorylation, or both.

The mechanisms of *absorption of fat* are also still controversial. Present evidence suggests that every single component of the digestion mixture— the partially hydrolyzed products (di- and monoglycerides), the completely hydrolyzed fat components (glycerol and fatty acids), as well as undigested fat molecules—can enter the intestinal cells, and that the split products are resynthesized within the cell to fat, which leaves the cell via the lymphatics. Furthermore, it seems that glycerol and the alkali salts of long- and short-chained fatty acids (soaps), being water-soluble compounds, can enter the epithelial cell by diffusion, and that the mono- and diesters of glycerol may cross the intestinal barrier without further cleavage, either in combination with bile components or on their own. All these split products are apparently re-esterified within the intestinal lining to triglycerides, and, as such, they leave the cell through the lacteals. It is possible that the pumping action of the villi plays a significant role in the transfer of the fat from the cells to the lacteals. In view of the prompt intracellular esterification of the split products, it is difficult to deçide whether or not unhydrolyzed fat particles pass through the cell membranes from the lumen, as was concluded from studies with radioactive carbon (C^{14}) incorporated into fat or its split products. Bile not only is important for the emulsification of ingested fat (see above), but it also serves as the carrier for the water-insoluble or less soluble components in the digestion mixture. Insoluble soaps, the monoglycerides, are probably "ferried" through the cellular barrier by bile acids in the form of chemical complexes, which separate in the cell spontaneously or by some unknown cellular activity. Some of the bile salt–bound fatty acids may pass through the cell unchanged and continue to the portal vein. This route may also be used by some of the triglycerides from short-chain fatty acids; by glycerol, which has not been employed in the cellular resynthesis of fat; and by the bile salts split off in the cell from fatty acids, soaps, and monoglycerides. By far the greater part of the fat or fat components proceed in the form of chylomicra into the lymphatics.

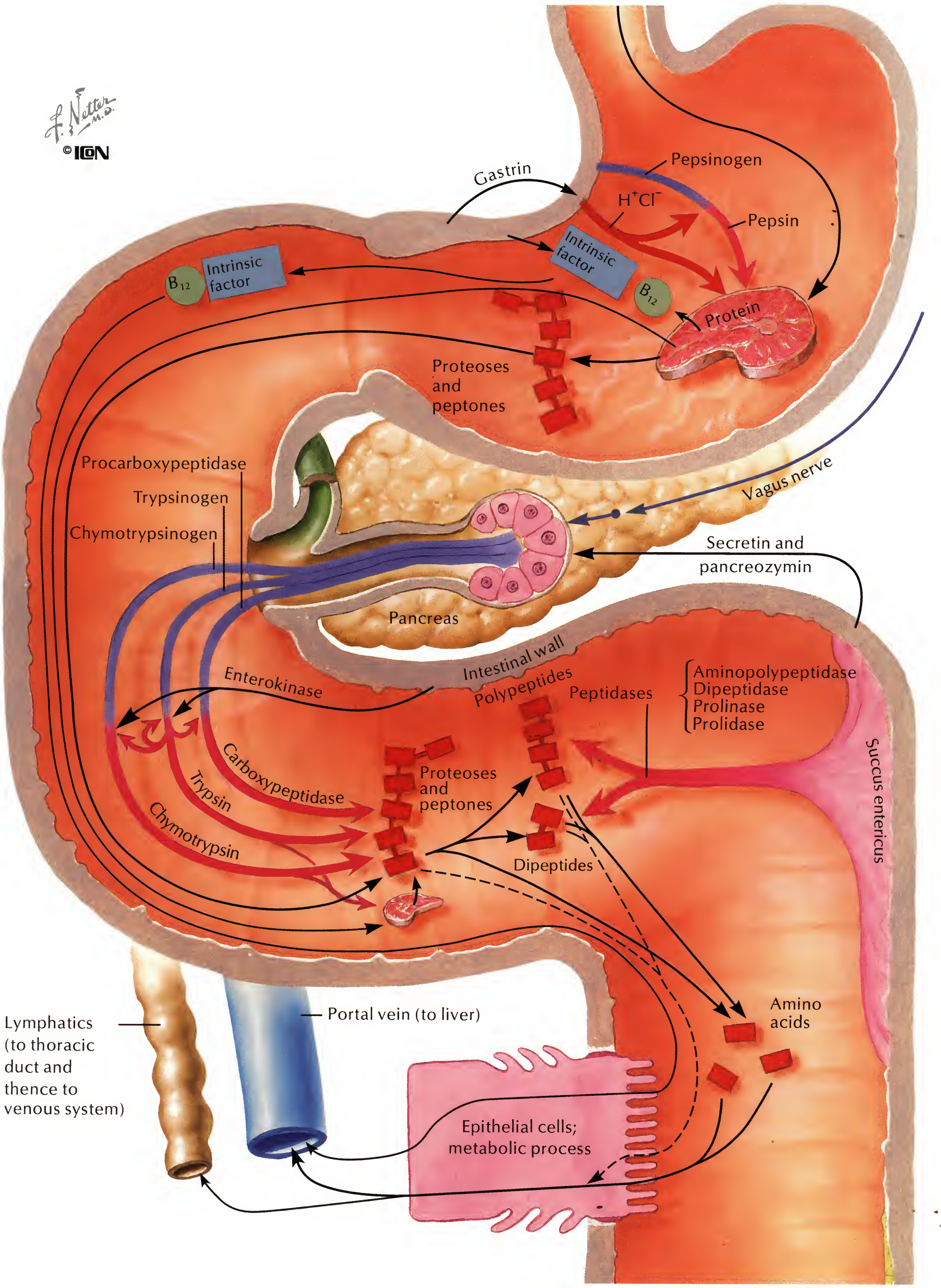
The absorption of other lipids, cholesterol, phosphatides, and fat-soluble vitamins is intimately related to the mechanisms of fat absorption. *Cholesterol* may be esterified in the lumen and may enter the cells in a bile-ester combination, or it may enter the cell as a bile complex and be partly esterified there. Free cholesterol and the cholesterol esters leave the intestinal cells by way of the lymph stream.

The absorption of the hydrolytic products of phospholipid digestion (see above) follows the line indicated for fat absorption. The evidence relating to the *absorption of vitamin A* suggests that, within the intestinal cell, carotene, the provitamin, may form a protein complex that passes into the blood or may be converted to a free vitamin, which is then esterified and passed on to the lymphatics. As to the absorption of vitamin D, little is known except that it requires the presence of bile and pancreatic juice. The same holds true for the absorption of vitamin E (tocopherol) and vitamin K (K_1 and K_2). Most vitamin K deficiencies are conditioned by the lack of bile salts.

The exact mechanisms involved in the absorption of the water-soluble vitamins (thiamine, riboflavin, nicotinic acid, pyridoxine, pantothenic acid, ascorbic acid, and cyanocobalamine [B_{12}]) are not entirely known, except for the fact that an intrinsic factor secreted by the gastric mucosa is necessary for the absorption of B_{12}.

Nonmotoric Functions of the Colon

The mucous membrane of the large intestine secretes an opalescent mucoid, *alkaline fluid* composed essentially of water, mucus, and some enzymes. Secretion of this fluid is enhanced by chemical and mechanical irritation. The colonic epithelium also has an excretory function insofar as it is used by the organism as an *elimination route for metals* (lead, mercury, bismuth, and, possibly, silver and calcium). The *digestive functions of the colon* are, under normal circumstances, of little practical significance but may become extremely significant as a compensatory mechanism when absorption in the small intestine is reduced by disease or surgical excision. Small amounts of starch, fat, and proteins, proteoses, peptones, and peptides, escaping digestion in the jejunum and ileum, may be digested in the colon, essentially by bacterial enzymes, which are capable of breaking down cellulose and other food components. The ability of *E coli* to split triglycerides is particularly noteworthy, because it makes the ratio of fat to fatty acids in the feces a rather unreliable index of pancreatic insufficiency. Certain amino acids, essentially *tryptophan*, but also *tyrosine*, *phenylalanine*, and *histidine*, yield, under the influence of bacterial enzymes, such compounds as *skatole*, *indole*, *phenol*, *cresol*, and *histamine*, respectively. These products of "putrefaction" may be absorbed in relatively small quantities by the mucosa and transported to the *liver*, where they are *detoxified*, to be excreted by the *kidney* in the form of *sulfates* and *glucuronides*. The bulk of material that remains in the colonic lumen and leaves the intestine with the feces contains indole and skatole, together with mercaptan and hydrogen sulfide, and bacterial decomposition products of cystine, which give the feces an unpleasant odor. The color of the feces derives chiefly from stercobilin, a bacterial reduction product of bile pigment. The important *absorptive faculty* of the large intestine, especially of the ascending colon, is concerned with the uptake of water, electrolytes, and a variety of water-soluble substances reaching the colon. These water-soluble substances also include some drugs (chloral hydrate, anticholinergics, xanthines, digitalis glucosides, etc.), which can, therefore, be administered rectally (by enema or suppositories). The water content of the fluid leaving the small intestine through the ileocecal valve is reduced about three- to fourfold as it passes through the ascending, transverse, and descending colon, leaving, under normal conditions, a rather concentrated mixture of mucus, solids deriving from indigestible food residues, and a great amount of bacteria.



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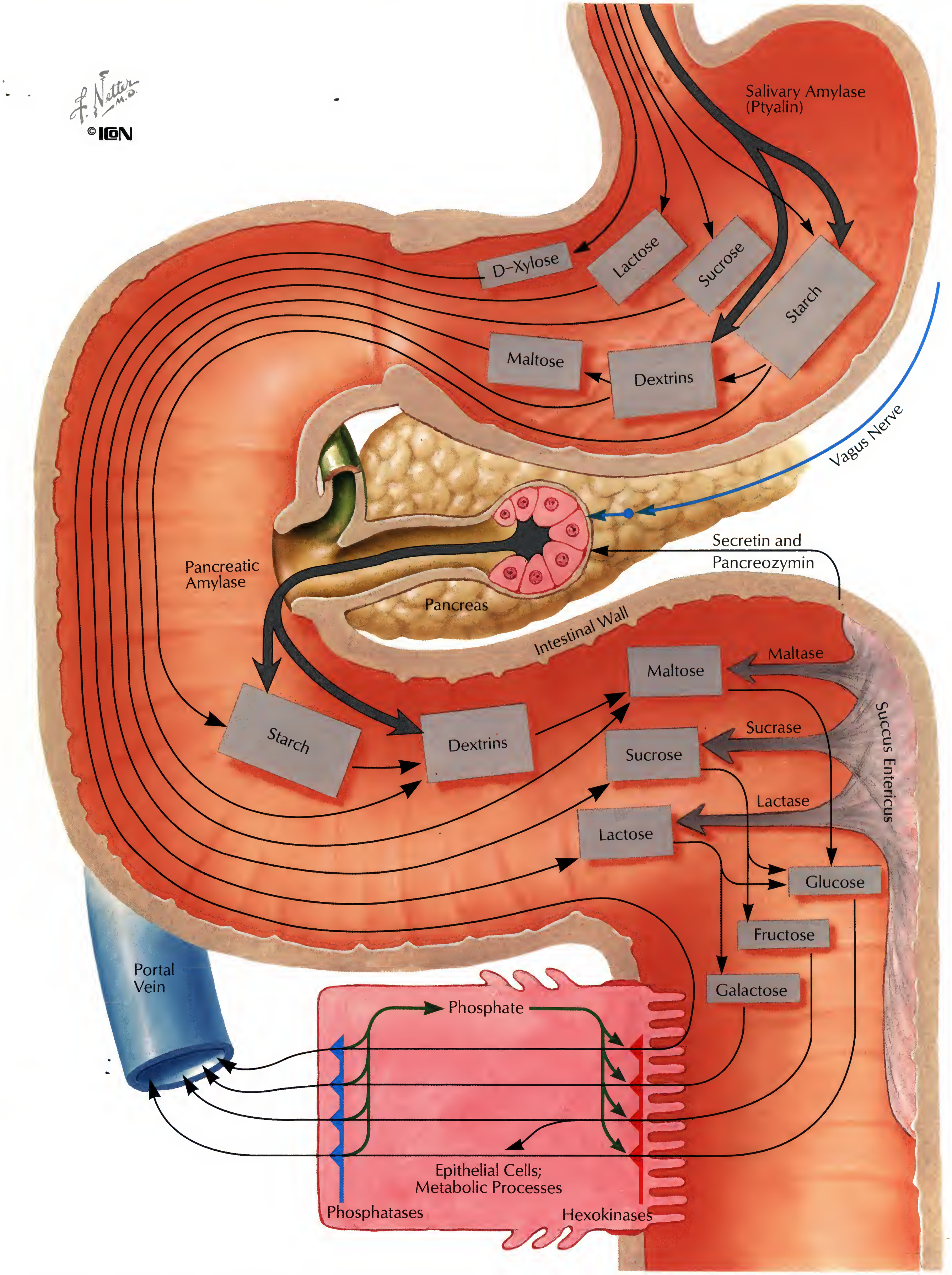
©ICON
Gastrin
Pepsinogen
H⁺Cl⁻
Pepsin
Intrinsic factor
B12
Intrinsic factor
B12
Protein
Proteoses and peptones
Procarboxypeptidase
Trypsinogen
Chymotrypsinogen
Vagus nerve
Secretin and pancreozymin
Pancreas
Intestinal wall
Enterokinase
Polypeptides
Peptidases
Aminopolypeptidase
Dipeptidase
Prolinase
Prolidase
Succus entericus
Carboxypeptidase
Trypsin
Chymotrypsin
Proteoses and peptones
Dipeptides
Amino acids
Lymphatics (to thoracic duct and thence to venous system)
Portal vein (to liver)
Epithelial cells; metabolic process



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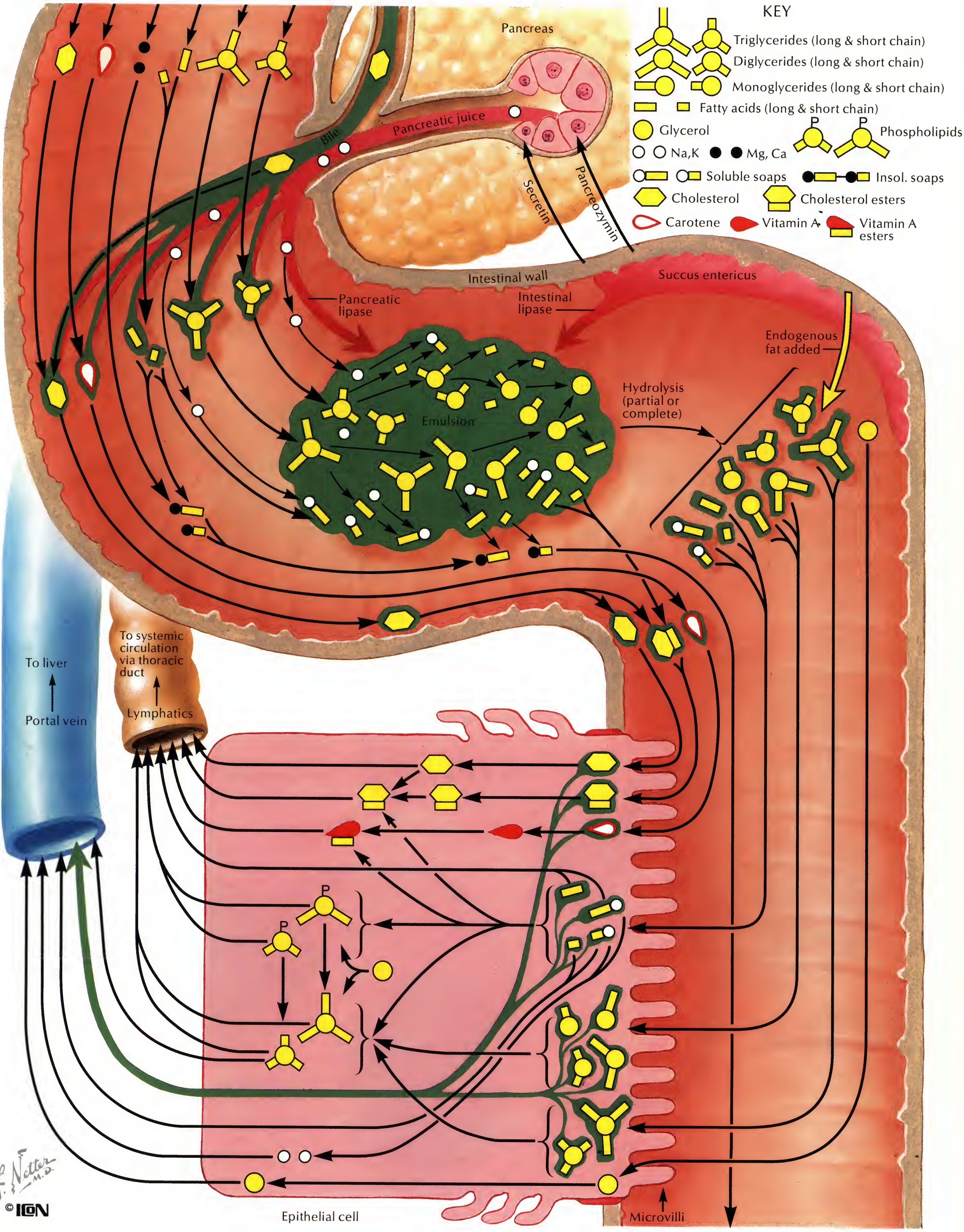
Salivary Amylase (Ptyalin)
D-Xylose
Lactose
Sucrose
Starch
Maltose
Dextrins
Vagus Nerve
Secretin and
Pancreozymin
Pancreatic Amylase
Pancreas
Intestinal Wall
Maltase
Maltose
Sucrase
Starch
Dextrins
Sucrose
Lactase
Lactose
Succus Entericus
Glucose
Fructose
Galactose
Portal Vein
Phosphate
Epithelial Cells; Metabolic Processes
Phosphatases
Hexokinases



KEY
Triglycerides (long & short chain)
Diglycerides (long & short chain)
Monoglycerides (long & short chain)
Fatty acids (long & short chain)
Glycerol
Phospholipids
Na,K
Mg, Ca
Soluble soaps
Insol. soaps
Cholesterol
Cholesterol esters
Carotene
Vitamin A
Vitamin A esters
Pancreas
Bile
Pancreatic juice
Secretin
Pancreozymin
Intestinal wall
Succus entericus
Pancreatic lipase
Intestinal lipase
Endogenous fat added
Emulsion
Hydrolysis (partial or complete)
To liver
Portal vein
To systemic circulation via thoracic duct
Lymphatics
P
Epithelial cell
Microvilli
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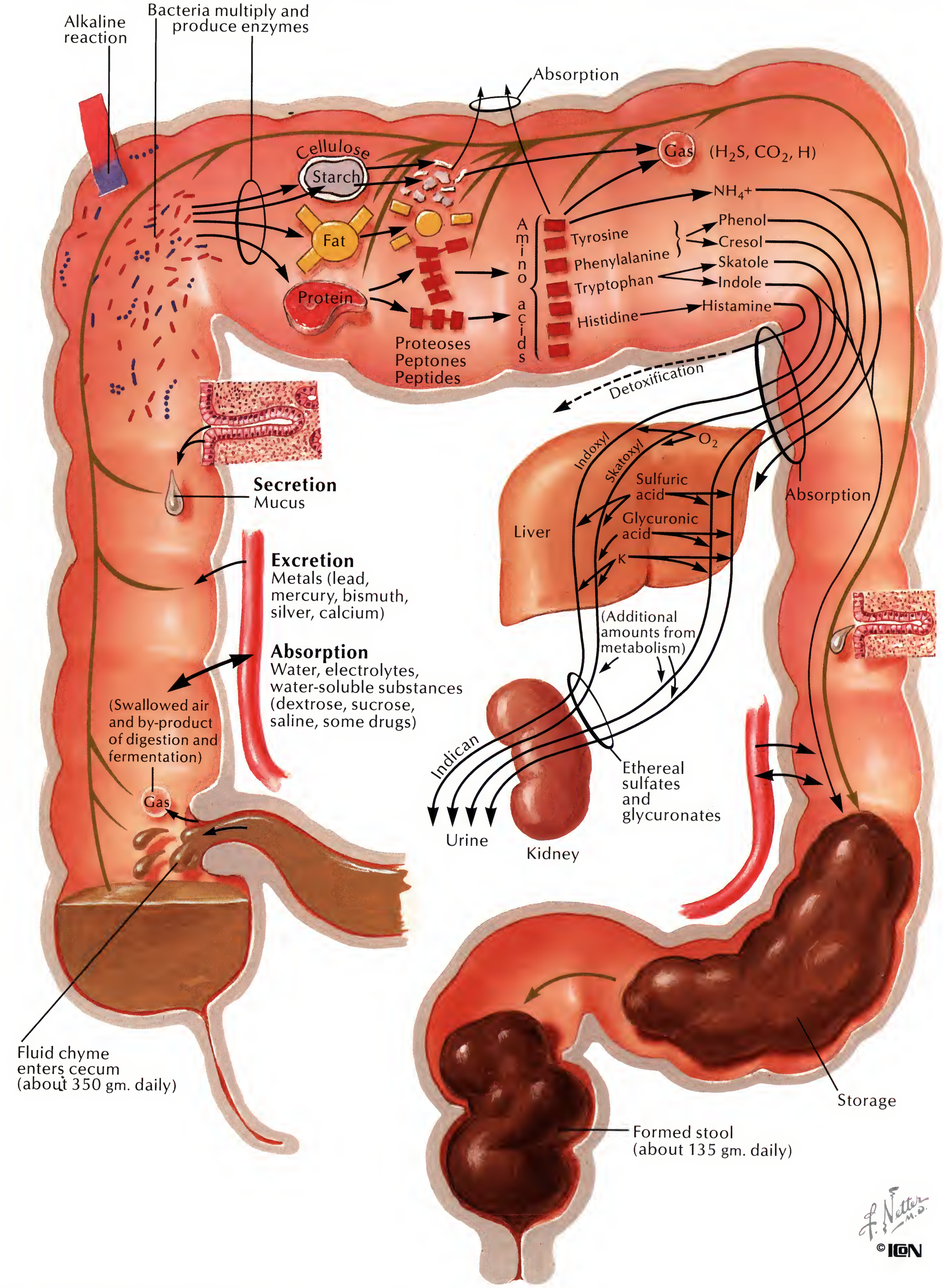
Secretory, Digestive, and Absorptive Functions (continued)



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